

REMARKS

Claims 1-90 are all the claims pending in the application.

The Examiner has indicated that none of the certified copies of the priority documents has been received.

Applicant has enclosed herewith the certified copies of the priority documents.

The Examiner has not explicitly indicated that the drawings filed on November 29, 2001 have been accepted.

The Examiner is respectfully requested to acknowledge acceptance of the drawings filed on November 29, 2001.

In the present Amendment, the specification has been amended to correct a clerical error by adding --5-Bromo-- for R₂ for compound No.47 in Table 1A on page 21. This is an obvious clerical error, and correction is supported by the name of the compound found, for example, at page 16, example 48 at page 62 and various claims.

Claims 1, 11-14, 26-29, 31-34, 36-39, 41-44, 50, 60-63, 65-69, 71-75, 83-84, 86 and 89-90 have been amended to delete non-elected subject matter.

Claims 1, 50, 65, 71, 83 and 89 have been amended to add --, and (v) at least one heteroaryl group is present--, to further limit the scope of the claims to the elected group.

Claims 83 and 85 have been amended to recite --inhibiting the formation of AGE-- and claims 1, 17, 19, 23-25 and 89 have been amended to recite --inhibiting the formation of AGE--. Support for this amendment is found, for example, at page 38, lines 5-6 of Applicants' specification.

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

Claim 77 has been amended to recite --wherein the carrier, diluent, excipient or solvent is one acceptable for oral administration--.

Claim 79 has been amended to recite --wherein the carrier, diluent, excipient or solvent is one acceptable for parenteral administration--.

Claim 81 has been amended to recite --wherein the carrier, diluent, excipient or solvent is one acceptable for use in lotion, oral rinse or toothpaste--.

Claims 60-63, 66-69 and 72-75 have been amended to replace "comprising compounds" with --wherein said compound is--.

Claim 49 has been amended to replace "a composition" with --said composition--.

Claims 17, 19, 24, 25 and 87 have been amended to replace "a compound" with --said compound--.

Claims 4-10, 53-59, 84 and 86 have been amended to replace "the said" with --said--.

Claims 1, 50, 65, 83 and 89 have been amended to replace "BF₄- and PF₆-" with -- BF₄⁻ and PF₆⁻--, and to recite --X is selected from the group--.

Claims 11-14, 26-29, 31-34, 36-39, 41-44, 60-63, 66-69, 72-75, 84 and 90 have been amended to add --and-- before the last listing compounds in the claims.

Claims 60, 84, 86, 90 have been amended to replace "pharmaceutially" with --pharmaceutically--.

Claims 17 and 23 have been amended to replace "atleast" with --at least--.

Claim 44 has been amended to replace "consistaing" with --consisting--.

Claims 50 and 89 have been amended to delete improper periods.

No new matter has been added. Entry of this Amendment is respectfully requested.

Upon entry of this Amendment, claims 1-14, 16-29, 31-34, 36-39, 41-44, 46-63, 65-69, 71-75, 77-81 and 83-90 are pending in the application.

I. Election/restrictions

The Examiner defined a genus from Applicants' election of compound No. 5. The genus is defined as follows: Group I, claims 1, 2, 4, 5, 7, 8, 10, 11, 16-26, 31, 36, 41, 46-50, 53, 54, 57, 59, 60, 65, 66, 71, 72 and 77-90 drawn to the composition of formula I in claim 1 where R_1 is $N(R_7)N(R_7)R_9$, R_7 is everything claimed except heterocyclic moieties, R_3 is everything claimed except heterocyclic moieties, X is everything claimed except heterocyclic rings, R_2 is everything claimed except heterocyclic rings, R_{10} , Y , R_{11} , R_{12} are as claimed.

The Examiner indicates that the nonelected portions of claims 1-90, as well as all of claims 3, 6, 9, 12-15, 27-30, 32-35, 37-40, 42-45, 51, 52, 55, 58, 61-64, 67-70 and 73-76 have been withdrawn from consideration as being drawn to a non-elected invention.

In the following reasons, Applicants respectfully submit that the Examiner has erred in defining the genus.

First, none of the claims recites that a substituent can be a heterocyclic group. However, the claims do recite that R_5 , R_7 , R_9 , and R_{10} can be "heteroaryl groups." Therefore, Applicants believe that the Examiner is referring to heteroaryl groups, not heterocyclic groups.

Second, the natural genus that the Examiner defined excludes the elected species Compound No. 5. More specifically, for Compound No. 5, R_3 is a heteroaryl group and X is

selected from the group consisting of a halide ion, acetate ion, perchlorate ion, sulfonate ion, oxalate ion, citrate ion, tosylate ion, maleate ion, mesylate ion, carbonate ion, sulfite ion, phosphoric hydrogen ion, phosphonate ion, phosphate ion, BF_4^- and PF_6^- .

However, the genus as defined by the Examiner wherein "R₃ is everything claimed except heteroaryl moieties" excludes Compound 5.

In addition, the definition of X as being "everything claimed except moieties forming heteroaryl rings" is inconsistent with the structure, because X, as defined in claim 1, is not such a group.

Further, in the present application, R₁ is only $\text{N}(\text{R}_7)\text{N}(\text{R}_7)\text{R}_9$. Therefore, Y, R₁₁ and R₁₂ are not present in the structure of formula I.

Accordingly, the Examiner is respectfully requested to define the natural genus to include Compound 5 as an element.

In a telephone communication with the Examiner on November 26, 2002, the Examiner suggested that Applicants respond such that the natural genus includes the elected species. The Examiner further advised that if the definition of the natural genus is inconsistent with the elected species, the next Office Action would be designated as non-final.

Accordingly, Applicants submit that in view of the elected species, it is reasonable to define Group I, the elected genus, in the manner as in amended claim 1, which includes all the compounds originally claimed and having the formula I where R₁ is $\text{N}(\text{R}_7)\text{N}(\text{R}_7)\text{R}_9$, R₂, R₃, R₇, R₁₀ and X are everything claimed, with the proviso that at least one heteroaryl group is present in the formula I.

In accordance with the definition above, Applicants note that, in addition to the claims identified by the Examiner as encompassing the elected subject matter, i.e., claims 1, 2, 4, 5, 7, 8, 10, 11, 16-26, 31, 36, 41, 46-50, 53, 54, 57, 59, 60, 65, 66, 71, 72 and 77-90, the elected subject matter is also encompassed by claims 3, 6, 9, 12-14, 27-29, 32-34, 37-39, 42-44, 52, 55-56, 58, 61-63, 67-69 and 73-75. Accordingly, Applicants respectfully request that these claims be included in the elected group.

II. Objection to Duplicate Claims

In the last paragraph at page 3 and the first two paragraphs at page 4 of the Office Action, the Examiner points out that claim 77 and claim 50, claim 79 and claim 50, and claim 81 and claim 50, are substantial duplicates, and advises that if any of claims 77, 79 and 81 is found allowable, claim 50 will be objected to.

In response, Applicants have amended claims 77, 79 and 81 to each recite an additional feature.

In view of Applicants' amendment, the Examiner is respectfully requested to reconsider and withdraw the objection.

III. Rejections Under 35 U.S.C. § 112, First Paragraph

A. In the paragraph bridging pages 4 and 5 of the Office Action, the Examiner rejected claims 1, 2, 4, 5, 7, 8, 10, 11, 16-25, 26, 31, 41, 46, 47-50, 53, 54, 56, 57, 59, 60, 65, 71, 72, and 77-90 asserting that there is no teaching of how to make and how to use compounds wherein R₅, R₇, R₉, R₁₀, and X are heteroaryl groups. The Examiner contends that it would require more than undue experimentation for one of ordinary skill in the art to determine how to

make and how to use compounds wherein the above-mentioned substituents can be any heteroaryl group.

First, Applicants submit that claims 11, 26, 31, 41, 72 and 90 do not recite any heteroaryl groups. Each of these claims recites specific compounds and, therefore, the above-mentioned substituents cannot be any heteroaryl group. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejection of claims 11, 26, 31, 41, 72 and 90.

Second, Applicants submit that X cannot be a heteroaryl group. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejection as to X.

In this Amendment, the structure of formula I, as amended, does not contain R₅. Accordingly, the examiner is respectfully requested to reconsider and withdraw the rejection as to R₅.

Applicants respectfully submit that a person of ordinary skill in the art will be in a position to make and use the compounds of formula (I) where R₇, R₉ and/or R₁₀ are heteroaryl groups without undue experimentation.

The following Schemes 1A, 2A and 3A describe the syntheses of the representative compounds having R₇, R₉ or R₁₀ as aromatic moieties. Schemes 1B, 2B and 3B describe the syntheses of corresponding compounds with heteroaryl moieties in R₇, R₉ and R₁₀, respectively.

Scheme - 1A

Having R₇ as aromatic moiety

Synthesis of alpha-chloroacetanilide i.e. compound (S)

To a stirred solution of aniline i.e. Compound (R) (23.25 gm, 0.25 mole) in tetrahydrofuran (100 ml) at 0 - 5 °C using an ice bath, triethylamine (34.78 ml, 0.25 mole) and chloroacetyl chloride i.e. Compound (Q) (19.92 ml, 0.25 mole) was added. The ice bath was removed and the solution was stirred for 1 hour. The reaction mixture was concentrated under vacuum to give a solid. The solid was taken into water (100 ml), stirred for 15 min. followed by filtration of the solid. Purification was carried out by crystallization from dichloromethane to get 28 gm of the solid of alpha-chloroacetanilide i.e. compound (S).

¹HNMR (DMSO d₆) 400 MHZ: 10.30 (1H,S), 7.60 - 7.58 (2H,d), 7.35 - 7.31 (2H, t), 7.11 - 7.07 (1H,t), 4.26 (2H,s).

Mass (M/Z) : 170, 171 and 172.

Synthesis of 1-(2-phenylamino-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium chloride i.e. Compound (65) from alpha-chloroacetanilide

To a solution of 3-(phenyl hydrazino carbonyl) pyridine i.e. compound (F) (1.0 gm, 0.0046 mole) in isopropyl alcohol (100 ml), alpha-chloroacetanilide, i.e., Compound (S) (0.85 gm, 0.0046 mole) was added. The solution was refluxed under stirring for 32 hours. The progress of the reaction was checked using thin layer chromatography.

The reaction mixture was filtered and the solid was crystallized using methanol (100 ml) to give 0.8 gm of solid 1-(2-phenylamino-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium chloride i.e. Compound (65).

The data for Compound (65) is given in the experimental section of the specification.

SCHEME - 1B

Having R₇ as heteroaromatic moiety

Synthesis of 2-chloro-N-pyridin-2-yl-acetamide i.e. compound (U)

For a chemist, who is aware of amide formation reactions, for example, reaction of chloroacetyl chloride (Compound (Q)) with aniline (Compound (R)) to get the respective condensation product i.e. amide, he / she can certainly, in analogy to said condensation reaction, carry out the condensation of chloroacetyl chloride (Compound (Q)) (the same compound used in the Scheme 1A) with 2-amino pyridine (Compound (T)) to get the respective condensation product 2-chloro-N-pyridin-2-yl-acetamide i.e. compound (U).

Synthesis of 1-(2-(2-pyridyl)amino-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium chloride i.e. Compound (V)

Further, using the quaternization procedure for preparation of Compound (65), a person skilled in the art can certainly prepare the respective quaternized compound i.e. 1-(2-(2-pyridyl)amino-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium chloride i.e. Compound (V) from 2-chloro-N-pyridin-2-yl-acetamide i.e. compound (U) and compound (F) (the same compound used in the Scheme 1A).

Please note that Compound (V) is not exemplified in the specification. However, as mentioned above a person skilled in the art can prepare the final Compound (V).

SCHEME - 2A

Having R₉ as aromatic moiety

Synthesis of 3-(phenyl hydrazinocarbonyl)-pyridine i.e. Compound (F)

In a round bottom flask, at 0 - 5 °C (using an ice bath), Phenyl hydrazine (Compound (G) (4 ml, 0.04 mole) in tetrahydrofuran (10 ml), nicotinoyl chloride (Compound (H))(5.6 gm, 0.04 mole) in tetrahydrofuran (40 ml), pyridine (10.5ml, 0.134 mole) were added. The ice bath was removed and the reaction mixture was stirred for 1 hour. The progress of the reaction was checked using thin layer chromatography.

The reaction mixture was filtered to get the solid and was further crystalized using methanol to get 0.93 gm. of the solid of 3-(phenyl hydrazinocarbonyl)-pyridine, i.e., Compound (F).

¹HNMR (DMSO-d₆) 400 MHz: 10.56 (1H,s), 9.09 (1H,s), 8.77-8.76 (1H,d), 8.27 - 8.25 (1H,d), 8.01 (1H,s) 7.57 - 7.54 (1H,q), 7.19 - 7.15 (2H,t), 6.82 - 6.80 (2H,d), 6.76 - 6.72 (1H,t)

Mass (M/z) : 214

Synthesis of 1-(2-ethoxy-2-oxoethyl)-3-(phenyl hydrazinocarbonyl)-pyridinium bromide i.e. Compound (78).

To a solution of 3-(phenyl hydrazinocarbonyl)-pyridine i.e. Compound (F)(1.5 gm, 0.007 mole) in isopropyl alcohol (15 ml), ethylbromoacetate (1.1 ml, 0.007 mole) was charged. The reaction mixture was refluxed and stirred for 18 hours. The progress of the reaction was checked using thin layer chromatography.

The reaction mixture was cooled to 0 - 5 °C using an ice salt bath to get a precipitate. The precipitate was taken into water (15 ml) and extracted with ethyl acetate (5 x 60 ml), followed by dichloromethane (5x60ml). The aqueous layer was concentrated under vacuum to

get 1.0 gm of solid i.e. 1-(2-ethoxy-2-oxoethyl)-3-(phenyl hydrazinocarbonyl)-pyridinium bromide i.e. Compound (78).

The data for Compound (78) is given in the experimental section of the specification.

SCHEME - 2B

Having R₉ as heteroaromatic moiety

Synthesis of 3-(2-(2-pyridyl)hydrazinocarbonyl)-pyridine . hydrochloride i.e. Compound (J)

To a cold solution (using an ice bath) of nicotiny chloride i.e. Compound (H) (207 gm, 1.46 mole) in tetrahydrofuran (650ml), triethylamine (289 ml, 2.07 mole) was added. 2-Hydrazino pyridine i.e. compound (I) (186 g, 1.70 mole) diluted in tetrahydrofuran (400 g) was added to the reaction mixture at 10 - 15°C. The ice bath was removed and the reaction mixture was stirred at room temperature for 4 hours. The progress of the reaction was checked using thin layer chromatography.

The reaction mixture was filtered and the filtrate was concentrated under vacuum to get crude material. To this crude material, methanolic HCl (400 ml) was added and stirred at room temperature for 1 hour to get the solid (31.0 gm).

¹HNMR (DMSO-d₆) 400 MHz: 11.46 (1H, s), 11.12 (1H, s), 9.293 - 9.289 (1H, d), 8.91 - 8.89 (1H, dd), 8.59 - 8.57 (1H, d), 8.15 - 8.06 (2H,m), 7.79 - 7.76 (1H, q), 7.39 - 7.31 (1H,d), 7.13 - 7.1 (1H,t)

Mass (M/z): 215, 216

Synthesis of 1-(2-ethoxy-2-oxoethyl)-3-(2-(2-pyridyl)hydrazinocarbonyl)-pyridinium bromide i.e. Compound (4) from Compound (J).

To a solution of 3-(2-(2-pyridyl)hydrazinocarbonyl)-pyridine . hydrochloride i.e. compound (J) (29 g, 0.116 mole) in dry ethanol (750 g), ethylbromoacetate (30ml, 0.232 mole) was charged. The reaction mixture was heated and stirred at 82 °C for 12 hours. The progress of the reaction was checked using thin layer chromatography.

The reaction mixture was cooled down to room temperature and the solid was filtered under vacuum. The solid was crystallized from methanol (250 ml) to give 11.5 gm white solid.

The data for compound (4) is given in the experimental section of the specification.

Scheme - 3A

Having R₁₀ as aromatic moiety

Synthesis of 3-(phenylcarbonyl hydrazino carbonyl) pyridine Compound (A)

In a round bottom flask, at 0 - 5 °C (using an ice bath) nicotinic hydrazide i.e. Compound (B) (20 gm, 0.145 mole) in tetrahydrofuran (350 ml.), triethyl amine (25 ml, 0.2 mole) and benzoyl chloride i.e. Compound (C) (19ml, 0.16 mole) in tetrahydrofuran (50 ml.) were added. The ice bath was removed and the reaction mixture was stirred for 2 hours. The progress of the reaction was checked using thin layer chromatography.

The reaction mixture was filtered and the solid was taken into water (50 ml) and stirred for 1 hour, filtered and dried to get 24.0 gm of 3-(phenylcarbonyl hydrazino carbonyl) pyridine i.e. Compound (A).

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

¹HNMR (DMSO-d₆) 400 MHz: 10.74 (1H,s), 10.61 (1H,s), 9.09 (1H,s), 8.8 - 8.78 (1H,m), 8.32-8.26 (1H,m), 7.95 - 7.93 (2H,d), 7.64 - 7.52 (4H,m)

Mass (M/Z) : 242

Synthesis of 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylcarbonyl hydrazino carbonyl) pyridinium bromide i.e. Compound (29)

To a solution of 3-(phenylcarbonyl) hydrazino carbonyl) pyridine i.e. Compound (A) (12.0 gm, 0.049 mole) in methanol (750 ml), 2-(alpha-bromo acetyl) thiophene (10 gm, 0.049 mole) was added. The reaction mixture was refluxed under stirring for 24 hours. The progress of the reaction was checked using thin layer chromatography.

The reaction mixture was cooled to 0 - 5 °C using an ice salt bath to get a precipitate. The precipitate was taken into water (500 ml) and extracted with ethyl acetate (5 x 600 ml). The aqueous layer was concentrated under vacuum to get a solid, which was crystallized from methanol : ethylacetate mixture to get 5 gm. of solid 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylcarbonyl hydrazino carbonyl) pyridinium bromide i.e. Compound (29).

The data for Compound (29) is given in the experimental section of the specification.

Scheme - 3B

Having R₁₀ as heteroaromatic moiety

Synthesis of 3-[(2-methoxy carbonyl)pyridine-5-yl-carbonyl] hydrazino carbonyl pyridine i.e. Compound (E)

In a round bottom flask, at 0 - 5 °C (using an ice bath), nicotinic hydrazide (Compound (B)) (2.8 gm, 0.02 mole), a solution of 6-carbomethoxy-nicotinoyl chloride (Compound (D))

(3.75 gm, 0.02 mole) in dry tetrahydrofuran (60 ml), and triethyl amine (3.8 ml, 0.027 mole) were added. The ice bath was removed and the reaction mixture was stirred for 3 hours. The progress of the reaction was checked using thin layer chromatography.

The reaction mixture was filtered to get a solid, and the solid was taken into water (25 ml) and stirred for 30 minutes, filtered to get 3.5 gm of 3-[(2-methoxy carbonyl)pyridine-5-yl-carbonyl] hydrazino carbonyl pyridine i.e. Compound (E).

¹HNMR (DMSO-d₆) 400 MHz: 10.96 (1H,s), 10.85 (1H,s), 9.17 (1H,s), 9.07 (1H,s), 8.79 - 8.77 (1H,m), 8.54 - 8.52 (1H,m), 8.28 - 8.27 (1H,m), 8.22 - 8.19 (1H,m), 7.60 - 7.56 (1H,m), 3.94 (3H,s).

Mass (M/Z): 301

Synthesis of 1-(2-thienyl-2'-yl-2-oxoethyl)-3-[(2-methoxy carbonyl)pyridine-5-yl-carbonyl] hydrazino carbonyl pyridinium chloride i.e. Compound (48)

To a solution of 3-[(2-methoxy carbonyl)pyridine-5-yl-carbonyl] hydrazino carbonyl pyridine i.e. Compound (E) (0.5gm, 0.002 mole) in methanol (15ml.) and isopropyl alcohol (15 ml.), and to it 2- (alpha-chloro acetyl) thiophene (1.5 gm, 0.009 mole) was added. The reaction mixture was refluxed under stirring for 96 hours. The progress of the reaction was checked using thin layer chromatography.

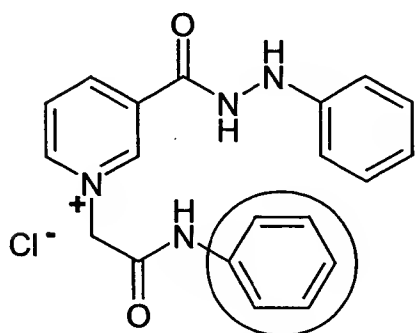
The reaction mixture was cooled to room temperature and the precipitated solid was filtered, and further washed with isopropyl alcohol (2x5ml). The solid was crystallized from isopropyl alcohol (5 ml) to give 0.26 gm of 1-(2-thienyl-2'-yl-2-oxoethyl)-3-[(2-methoxy carbonyl)pyridine-5-yl-carbonyl] hydrazino carbonyl pyridinium chloride i.e. Compound (48).

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appln. No. 09/995,731

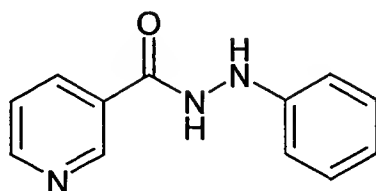
The data for Compound (48) is given in the experimental section of the specification.

The following schematic diagrams (schemes 1-3) show the route to be followed for syntheses of these compounds.

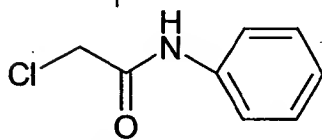
Scheme - 1A



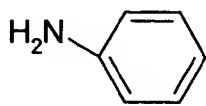
Compound No. 65



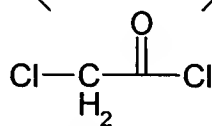
Compound (F)



Compound (S)

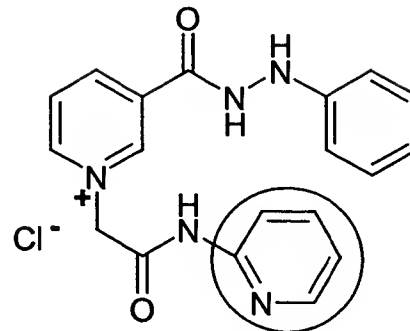


Compound (R)

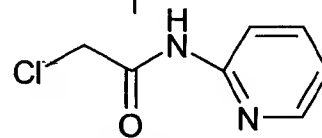


Compound (Q)

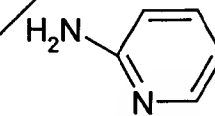
Scheme - 1B



Compound No. (V)

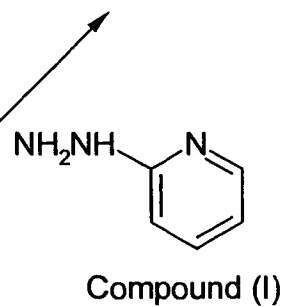
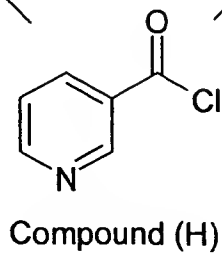
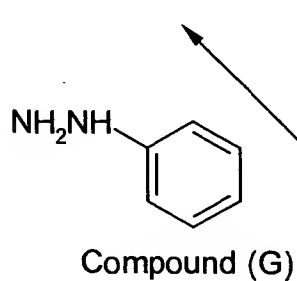
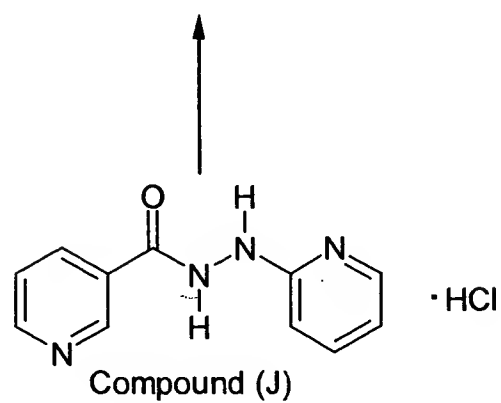
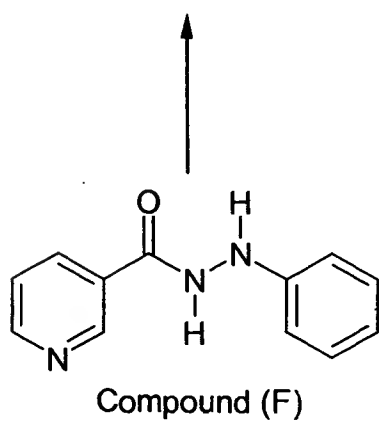
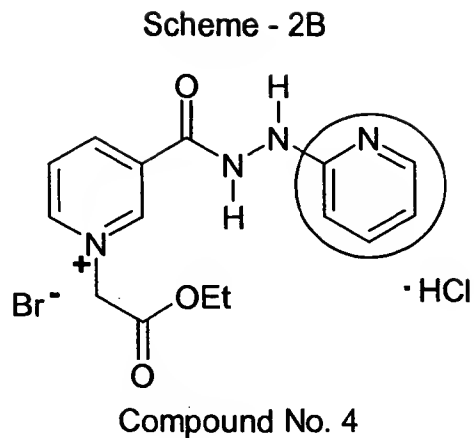
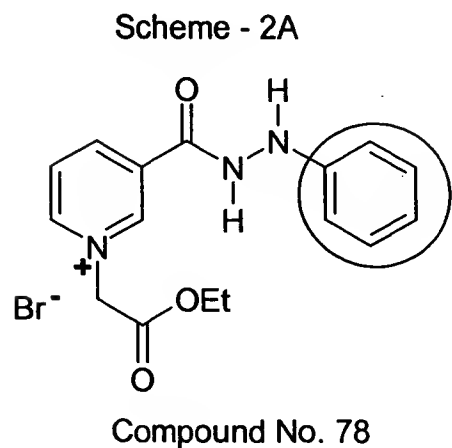


Compound (U)

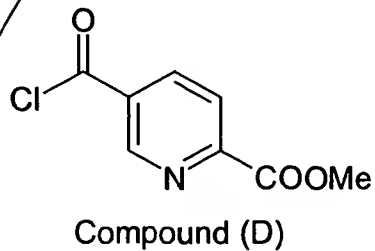
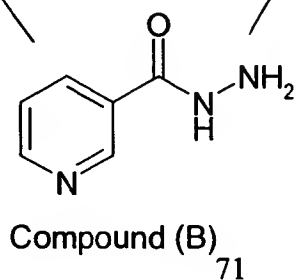
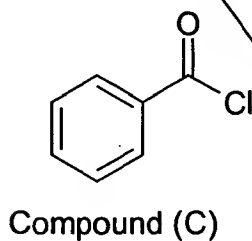
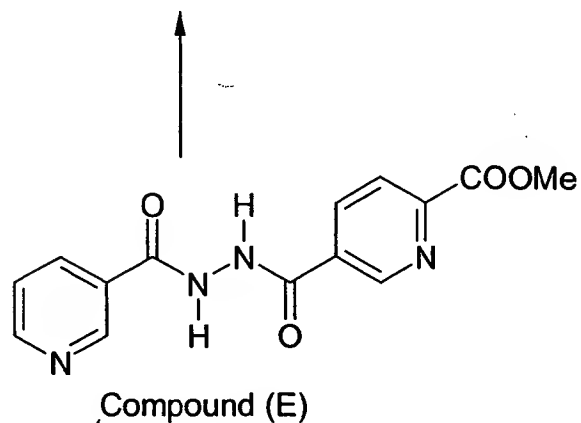
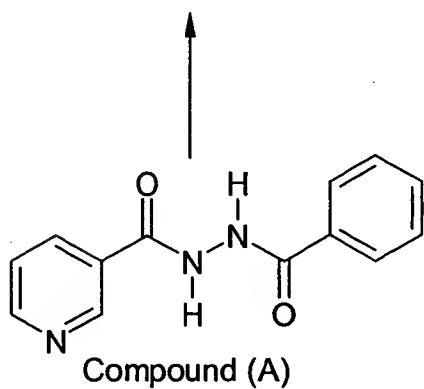
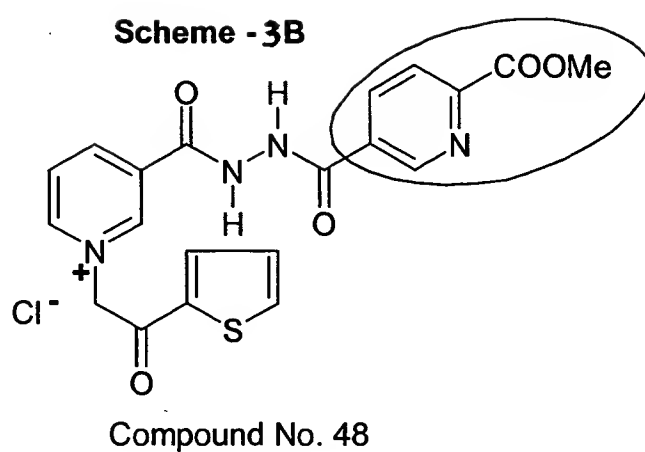
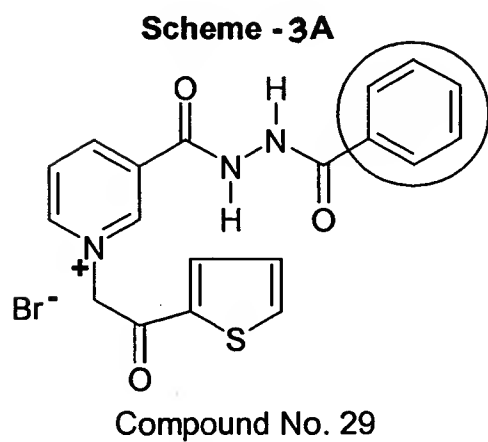


Compound (T)

Scheme - 2
For definition of R₉



Scheme - 3
For definition of R₁₀



From these schemes, it is apparent to a person of ordinary skill in the art, how to synthesize the compounds with heteroaryl substituent(s) of R₇, R₉ and/or R₁₀ without undue experimentation, from what is disclosed in the specification and what was known in the art at the time of the present invention.

In view of the above, the Examiner is respectfully requested to reconsider and withdraw the rejection.

B. In the first full paragraph at page 5 of the Office Action, claims 16 and 24 have been rejected as not being enabled for preventing diseases, claim 71 has been rejected as not being enabled for treating every disease caused by accumulation of free radicals, and claim 82 has been rejected as not being enabled for treating every disease (a) through (j), recited therein.

Applicants respectfully submit that the methods of preventing diseases recited in claim 16 and 24 are fully enabled by the specification.

Applicants respectfully draw the attention of the Examiner to the fact that as of the filing date of the instant application (29th November, 2001), there was wealth of data, in the form of peer-reviewed journal articles, showing a reasonable correlation between the formation of Advanced Glycation End products (AGE) and/or free radical and the indications recited in claims 16 and 24. Similarly a number of references teach that compounds with the ability to inhibit / break preformed AGE or which can be used to arrest the free radical, can be used for the indications recited in claims 16 and 24. These references are discussed in detail below. In contrast to the Examiner's position that the claims as recited are broader than the scope of the

enablement, it would be observed there is a clear support for the utility of the claimed invention towards the indications as recited therein.

Further, although, Applicants agree with the Examiner that most of the drugs are used to treat diseases rather than prevent diseases (page 5 paragraph 2 of the Office Action), based on the disclosure of the present invention and the knowledge of the skilled artisans at the time of the invention, as evidenced from the documents discussed below, the skilled artisan would have been able to use the compounds of the instant invention also towards the prevention of the indications recited in claims 16 and 24.

Background:

As explained by Boni et al. (Boni R. Burg G.; Schweix Med Wochenschr (2000) September 9; 130(36):1272-8), skin represents the most viable organ of aging showing manifestations like wrinkles, senile xerosis, loss of skin tone and the like. Cutaneous aging is a complex phenomenon consisting of intrinsic aging and extrinsic aging. A number of biological changes can be found during the cutaneous aging process including a decrease of epidermal and dermal components. (Boni R. Burg G.; Schweix Med Wochenschr (2000) September 9; 130(36): 1272-8).

The cross linking that occurs between glucose and polypeptide chains has been well recognized. Such reactions are known to occur in variety of proteins such as collagens (Dyer DG et al. J. Clin. Invest 1993 Jun;91(6):2463-9, Verzijl Nicole, The Journal of Biological Chemistry, Page 39027 - 39031, Vol 275, No. 50, Dec. 2000). These reactions are accelerated in the presence of elevated glucose, but may also occur under normal glucose levels. The products

of such reactions are termed Advanced Glycation Endproducts. As described in US patent nos. 5,656,261 (issued August 12, 1997) and 5,853,703 (issued December 29, 1998) agents and methods are disclosed which reverse (or cleave or break) AGE formation *in vitro* and *in vivo*.

Co-pending U.S. application No. 09/590,143 (allowed), from which the instant application is a continuation-in-part, discloses the use of the compounds of the invention as breakers of Advance Glycation End-Products (AGE). Also, as exemplified in the instant specification, the compounds have free radical scavenging activity as well as Advanced Glycation End product (AGE) inhibitor properties. The indications of aging / skin related conditions are directly associated with AGE and / or free radicals, whereas the compounds of the present invention have the AGE breaker / inhibitor property and free radical scavenging property. Hence one can clearly understand that the compounds of the present invention can be useful for treatment as well as prevention of the indications recited in Claims 16 and 24. Aging is a biological phenomenon which is characterized by wrinkles, sagging skin, skin discoloration, age spots, dry spots, blemishes, skin texture, skin tone etc. As shown below, the method as claimed in claims 16 and 24 can be practiced without undue experimentation.

a & b) Reversal and prevention of wrinkles and fine lines

That proteins cross link as a consequence to AGE formation, is important since it is responsible for wrinkling. The studies on the role of AGEs in aging collagen using a scanning force microscope reveal that in the presence of an increased concentration of AGEs, significant structural alteration has been observed in the collagen fibrils of old rats (Odetti P, Aragno I, et al.

: Role of advance glycation end products in aging collagen. A scanning force microscope study; Gerontology (1998); 44 (4): 187-91).

Wagle DR et al. (US 6121300 dated September 19, 2000) have clearly indicated that the compounds having AGE breaker property can be useful for reversing the aging of key proteins and thus improving skin elasticity or reducing wrinkle.

Further, it should be noted that photo-aging resulting in an induction of matrix metalloproteinases and a subsequent un-balanced production of metalloproteinases over anti-metalloproteinases induced by free radicals leads to breakdown of collagen and elastin of skin (Berneburg M, Plettenberg H, Krutmann J : Photoaging of human skin: Photodermatol. Photoimmunol. Photomed. (2000): 16: 238-44). This is followed by imperfect wound repair of the damaged collagenous matrix and accumulation of elastic material. As a consequence the skin sags and wrinkles. It is also known that antioxidants are essential in protecting the epidermis from damage by free radicals generated both by environmental and endogenous factors (Pugliese PT: The skin's antioxidant systems Dermatol.Nurs (1998) Dec: 10 (6): 401-16; quiz 417-18). The studies have proven that UV radiation increases the formation of AGEs on collagen, elastin and other skin proteins. It is also reported that AGE is an important factor for promoting photoaging in the skin (Masaki H, Okano Y, Sakurai H : Generation of active oxygen species from advanced glycation end products (AGE) under ultraviolet light A (UVA) irradiation: Biochem. Biophys.Res.commun. (1997) Jun 18: 235). Skin aging is manifested by normal or small (fine) wrinkles (US 6224850). Deep wrinkles occur due to photoaging of the skin (Hitoshi Masaki et. al.; Biochem. Et Biophysica Acta (1999) 45-56).

Duffy et al. (WO 01/62247 A1) have clearly indicated that wrinkles and fine lines can be reduced by using thiazolium compounds. Further, it needs to be noted that the thiazolium compounds are prepared according to the procedures described in US Patent No. 5,656,261, and also they have AGE-inhibitor properties. Thus, the AGE formation is inhibited and the wrinkles are reduced. Hence, if the existing AGE is broken, then the wrinkles can even be prevented.

Thus, if the total tissue burden of AGE is controlled, then the wrinkles and fine lines can be reversed or prevented. The compounds of the present invention have the ability to inhibit the formation of AGEs along with AGE breaker activity (See U.S. Appln. No. 09/590,143 filed on June 9, 2000 and is now allowed by the US PTO), and, hence, the compounds of the present invention are capable of reversal and prevention of wrinkles and fine lines as claimed in claims 16 and 24.

c) Promotion of epidermal growth

The co-relation between aging skin and epidermal is well documented by Boni et al. (Boni R. Burg G.; Schweix Med Wochenschr (2000) September 9, 130(36):1272-8). A number of biological changes can be found during the cutaneous aging process including a decrease of epidermal and dermal components.

As explained by Pugliese PT (Dermatol Nurs 1998 Dec, 10 (6) 401-16, quiz 417-8) anti-oxidants are essential in protecting the epidermis from damage by free radicals generated both by environmental and endogenous factors.

As explained in items (a) and (b) above, aging is related to Advanced Glycation Endproduct. Furthermore, AGE accumulates (Jeanmaire C. et al. British Journal of

Dermatology, 2001: 145; 10-18) (accepted for publication March 1, 2001 and published before the actual U.S. filing of the instant application) upon aging, playing a part in tissue stiffening and elasticity, which is related to epidermis.

The compounds of the present invention also work as free radical scavenger as well as AGE inhibitors / breakers and hence show activity for promotion of epidermal growth.

d) Photo protection of skin

Photoaging of skin is characterized by many symptoms. When elicited by UVB exposure, concentrations of AGEs have been reported in the human photo-aged dermis (M. Naganuma; Shiseido Co., LTD, Tokyo, Japan, International Congress on Photobiology, 28th Annual American Society for Photo Biology Meeting, San Francisco, California, USA, July 1-6, 2000, Paper 404; Herfindal et. al., Clinical Pharmacy and Therapeutics, page 753, 5th Edition, Williams & Wilkins 1992). Antioxidants are essential for protecting dermis from damage by free radicals (Pugliese P T: Dermatol. Nurs (1998) December: 10 (6): 401-16).

AGE is an important factor for promoting photoaging in the skin. Also, free radicals add on to the photoaging process (Masaki H et al. Biochim Biophys Acta 1999 Jun 28; 1428(1): 45-56, Masaki H et al. Biochem Biophys Res Commun 1997 June 18; 235 (2): 306-10).

Thus, a composition with active molecules of the instant invention, which is capable of inhibiting and breaking the AGE cross links and creating an anti-oxidative environment in tissues, significantly slows down the photoaging manifestation.

e, f & g) Reversal and prevention of skin discoloration, age spots and dryness

The co-relation between thiazolium compounds (which control the content of AGE in the tissues) and skin discoloration, age spots and dryness of skin (skin clarity) is well documented by Duffy et al. (WO 01/62247 A1). Thus, if the compounds having AGE inhibitor / breaker properties are used in the compositions, when applied on the skin, the skin discoloration, age spots and dryness can be reversed or prevented. Hence, the compounds of the present invention having AGE-inhibitor / breaker property can certainly be useful for the same.

h & i) Reversal and prevention of stretch marks and blemishes

Skin aging is a complex phenomenon resulting from the interaction of several internal and external factors. Recent studies have demonstrated that Advanced Glycosylation Endproducts (AGE) crosslink formation and free radical formation are key mechanisms involved in skin aging and wrinkle formation. During the course of chronological aging, the skin support proteins, like collagen and elastin, get cross linked with AGE (Verzija Nicole, The Journal of Biological Chemistry, Page 39027 - 39031, Vol 275, No. 50, Dec. 2000) leading to a loss of suppleness and elasticity of the skin (WO 01/62247 A1), and resulting in accelerated skin aging and wrinkle formation. The compounds of present invention are expected to restore the elasticity and suppleness of the skin by breaking AGE cross-links (in the skin support proteins) and preventing the deleterious effects of free radicals. By virtue of restoring the elasticity of skin the compounds of the present invention are expected to reverse or prevent the stretch marks and reduce blemishes of the skin.

Stretch marks are a common disfiguring condition associated with continuous and progressive stretching of the skin, for example, which occurs during pregnancy. The

pathogenesis of stretch mark relates to changes in those structures that provide skin with its tensile strength and elasticity, which in turn is related to fibrillin, elastin and collagens from the skin. Light microscopy reveals an increase in glycated proteins (AGE) from the region of stretch marks (Watson RE et al. Br J Dermatol 1998 Jun; 138(6): 931-7).

Thus, the compounds of the invention having AGE breaker / inhibitor / free radical scavenger activities are expected to have beneficial effects on stretch marks and blemishes.

j) Skin care and skin conditioning

The co-relation between thiazolium compounds (which control the content of AGE in the tissues) and skin firmness / plumpness etc., which directs towards skin care and conditioning is well documented by Duffy et al. (WO 01/62247 A1). Thus, if the compounds having AGE inhibitor / breaker properties are used in the compositions, which can be applied on the skin, skin care and conditioning can occur.

Skin, which has a highly differentiated and certainly complex organizational structure, is particularly vulnerable to free radical damage (Calabrese V et al. Drugs Exp Clin Res 1999; 25(6): 281-7).

Thus, the compounds of the present invention, which also have the property of free radical scavenger and AGE inhibitor / breaker, are useful for skin care and conditioning.

k) Reversal and prevention of senile xerosis

As explained by Boni et al. (Boni R. Burg G.; Schweiz Med Wochenschr (2000) September 9; 130(36): 1272-8), skin represents the most viable organ of aging showing manifestations as senile xerosis.

Cutaneous aging is a complex phenomenon consisting of intrinsic aging and extrinsic aging. A number of biological changes can be found during the cutaneous aging process including a decrease of the epidermal and dermal components. (Boni R. Burg G.; Schweix Med Wochenschr (2000) September 9; 130(36): 1272-8). Thus, senile xerosis is caused by photoaging, whereas AGE is an important factor for promoting photoaging in the skin. Also, free radicals add on to the photoaging process (Masaki H et al. Biochim Biophys Acta 1999 Jun 28; 1428(1):45-56, Masaki H et al. Biochem Biophys Res Commun 1997 June 18; 235 (2): 306-10).

l) Conditioning and prevention of sun burns

In sunburn, when elicited by UVB exposure, concentrations of AGEs have been reported in the human photoaged dermis (M. Naganuma; Shiseido Co., LTD, Tokyo, Japan, International Congress on Photobiology, 28th Annual American Society for Photo Biology Meeting, Sanfransico, California, USA, July 1-6, 2000, Paper 404; Herfindal et. al. Clinical Pharmacy and Therapeutics, page 753, 5th Edition, Williams & Wilkins 1992).

Antioxidants are essential for protecting dermis from damage by free radicals (Pugliese P T: Dermatol. Nurs (1998) December: 10 (6): 401-16). Hence, a cosmetic application with active molecules of the instant invention is capable of reversing the AGE cross links and creating an anti-oxidative environment in tissues through its AGE breaking and free radical quenching actions, thereby conditioning and preventing sun burns.

m, n, o & p) Preventing and reversing the loss of collagen, improving skin texture, skin tone and enhancing skin thickness

Collagen fibers are responsible for the strength of the dermis and participate in the tonicity of the skin. Collagen fibers are regularly renewed. A decrease in the renewal of these collagen fibers causes thinning of the dermis. In dermal components of the skin glycation occurs particularly in the dermis, on the collagen fibers (EP 1110539 A1, dated 27th June, 2001 (this EP patent is not in English, therefore, the corresponding US 6,414,038 patent, dated July, 2, 2002, is submitted herewith). Improved collagen turnover is expected to improve the tone and luster of the skin.

The cross linking that occurs between glucose and polypeptide chains has been well recognized. Such reactions are known to occur in a variety of proteins, such as collagens (Dyer DG et al. J. Clin. Invest 1993 Jun; 91(6):2463-9, Verzijl Nicole, The Journal of Biological Chemistry, Page 39027-31, Vol 275, No. 50, Dec. 2000). These reactions are accelerated in the presence of elevated glucose, but may also occur under normal glucose levels. The products of such reactions are termed as Advanced Glycation Endproduct. As described in US patent nos. 5,656,261 (issued August 12, 1997) and 5,853,703 (issued December 29, 1998), agents and methods are disclosed which reverse (or cleave or break) AGE formation *in vitro* and *in vivo*.

The compounds of the present invention are useful as breakers of Advanced Glycation Endproduct (AGE) (1st CIP US application no. 09/590,143 filed on June 9, 2000 in this series and now accepted). Also, as exemplified in the instant specification, the compounds have free radical scavenging activity as well as Advanced Glycation Endproduct (AGE) inhibitor property. The indications of aging / skin relation are directly associated with AGE and/or free radicals. In view of the fact that the compounds of the present invention have AGE breaker / inhibitor

properties / free radical scavenging property, one can clearly understand that the compounds of the present invention can be useful for treatment as well as prevention of the indications from Claims 16 and 24.

The AGE breaker compounds of the instant invention would reduce the AGE mediated damage to the skin supporting proteins (elastin and collagen).

Thus, the composition containing a compound of the instant invention can be used for preventing and reversing the loss of collagen, improving skin texture and skin tone, and enhancing skin thickness.

q) Decreasing pore size

Duffy et al. (WO 01/62247 A1) have clearly indicated that pore size can be reduced by using thiazolium compounds. Further, it needs to be noted that the thiazolium compounds are prepared according to the procedures described in US Patent No. 5,656,261, and, also they have AGE-inhibitor property.

Thus, if the total tissue burden of AGE is controlled, the pore size can be reduced. The compounds of the present invention have the ability to inhibit the formation of AGEs along with AGE breaker activity (See application no. 09/590,143 filed on June 9, 2000, allowed). Hence, the compounds of the present invention are capable of reducing pore size as claimed in claim 16 (q).

r, s & t) Restoring skin luster, minimizing signs of fatigue and reducing acne

Duffy et al. (WO 01/62247 A1) have clearly indicated that restoring of skin luster, minimizing signs of fatigue and reducing acne can be achieved by using thiazolium compounds.

Further, it needs to be noted that the thiazolium compounds are prepared according to the procedures described in US Patent No. 5,656,261, and, also that they have AGE-inhibitor properties.

Thus, if the total tissue burden of AGE is controlled, then the restoration of skin luster, minimizing signs of fatigue and reducing acne can be achieved. The compounds of the present invention have the ability to inhibit the formation of AGEs along with AGE breaker activity (See application no. 09/590,143 filed on June 9, 2000, allowed). Hence, the compounds of the present invention are capable of restoring the skin luster, minimizing signs of fatigue and reducing acne as claimed in claim 16 (r), (s) & (t) respectively.

u) Treatment of Telangiectasia

Photoaging is characterized by many symptoms including Telangiectasias. When elicited by UVB exposure, concentrations of AGEs have been reported in the human photoaged dermis (International Congress on Photobiology, 28th Annual American Society for Photo Biology Meeting, Sanfransico, California, USA, July 1-6, 2000, Paper 404, M. Naganuma; Shiseido Co., LTD, Tokyo, Japan; Clinical Pharmacy and Therapeutics, page 753, 5th Edition, 1992).

Antioxidants are essential for protecting dermis from damage by free radicals (Pugliese P T: Dermatol. Nurs (1998) December: 10 (6): 401-16). Hence, a cosmetic application with active molecules of the instant invention is capable of reversing the AGE cross links and creating an anti-oxidative environment in tissues through its AGE breaking and free radical quenching actions, thereby significantly treating Telangiectasia.

Telangiectasia is a condition characterized by the dilation of one or more superficial arterioles in the human body, such that the effected arterioles become visible through the skin. There are invasive techniques available to treat Telangiectasia. Recently, WO 01/62247 A1 disclosed a topical composition containing thiazolium (which inhibit / reverse AGE formation) compounds for treatment of Telangiectasia.

The compounds of the present invention break the AGE cross-links and thereby are expected to restore elasticity, size and shape of the affected arterioles. By virtue of this, the compounds of the present invention are expected to show a beneficial effect in Telangiectasia.

v) Improving aesthetic appearance of hair and nail

Glycation of proteins, which is a universal phenomenon and well known for the skin, particularly for its components, also occurs in the annexes or related structures thereof such as the nails or the hair, particularly on the keratins and more generally in any protein system if the conditions required for glycation exist (EP 1110539 A1, dated 27th June, 2001) (this EP patent is not in English, therefore, the equivalent US Patent No. 6,414,038, dated July, 2, 2002, is submitted herewith).

Kobayashi et al (Biol Pharm Bull 1996 Apr; 19(4): 487-90) have proposed Glycation index of hair as an indicator for diabetic control that shows the extent of glycation of hair protein (keratin).

The compounds of present invention having AGE breaker / inhibitor activity are expected to demonstrate a beneficial effect on hairs and nails by breaking the AGE cross links formed in hairs and nails.

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appln. No. 09/995,731

Regarding claims 71 and 82, Applicants submit that the disclosure of the present application provides sufficient enablement for the method of treating all diseases claimed in claims 71 and 82. For example, at pages 87-94, it is indicated that the compounds of the present invention have free-radical scavenging activities and that they can be used in controlling oxidative stress for effective management of conditions, such as those claimed in claim 82.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejection.

C. In the last full paragraph at page 5 of the Office Action, the Examiner states that the specification does not enable inhibiting "AGE." The Examiner states that AGE is a mechanism and therefore cannot be correlated with a specific disease.

Applicants respectfully submit that Applicants' specification enables the inventions claimed in claims 83 and 85 as amended. Specifically, the specification discloses a method of and a composition for inhibiting the formation of AGE.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejections under 35 U.S.C. §112, first paragraph.

IV. Rejections Under 35 U.S.C. § 112, Second Paragraph

A. At page 7, third full paragraph, labeled "A," the Examiner states that in claim 1, and all other claims where applicable, the phrase "and a pharmaceutically acceptable carrier" should be inserted, as the claims are composition claims.

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appln. No. 09/995,731

Applicants respectfully submit that appropriate carriers have been recited in each of the claims. For example, claim 1, line 12, recites a cosmetically acceptable carrier, claim 50, line 14, recites a pharmaceutically acceptable carrier, and claims 50, 65, 71, 83 and 89 recite pharmaceutically acceptable carriers.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejection.

B. At page 7, fourth full paragraph, claim 72 has been rejected for lack of antecedent basis for the word "compounds".

In response, Applicants have amended claims 72 and all other claims where applicable, i.e., claims 60-63, 66-69 and 73-75, to replace "comprising compounds" with --wherein said compound is--.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejection.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appln. No. 09/995,731

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

SUGHRUE MION, PLLC
2100 Pennsylvania Avenue, N.W.
Washington, D.C. 20037-3213
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

Fang Liu, Reg. No 51283
for Susan J. Mack
Registration No. 30,951

Date: January 3, 2003

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appln. No. 09/995,731

APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

At page 21, the table is amended as follows:

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

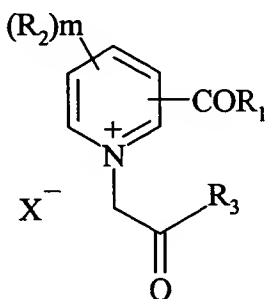
Compd. No.	R ₁	m	-R ₂	-R ₃	-X
30	NHNHSO ₂ CH ₂ Ph	0	-	OEt	Br
31	NHNHSO ₂ CH ₂ Ph	0	-	-Ph	Br
32	Structure (e)	0	-	2-furyl	Br
33	Structure-(f)	0	-	2-thienyl	Cl
34	NHNHCOCH ₂ CH ₂ -cyclohexyl	0	-	2-thienyl	Br
35	NHNHCOCH ₂ CH ₂ -cyclohexyl	0	-	-NHPh	Cl
36	NHCH ₂ CH ₂ OCO-phenyl	0	-	2-thienyl	Br
37	NHCH ₂ CH ₂ OCO-phenyl	0	-	CH ₂ CO ₂ -ethyl	Cl
38	-NHCH ₂ CH ₂ OCH ₃	0	-	-2,4-dichlorophenyl	Br
39	Structure-(g)	0	-	NH-cyclopropyl	Cl
40	-NHCH ₂ CH ₂ OCH ₃	0	-	NH-cyclopropyl	Cl
41	Structure-(h)	0	-	NH-isopropyl	Cl
42	Structure-(i)	0	-	2-thienyl	Cl
43	NHNHSO ₂ CH ₃	0	-	NH-isopropyl	Cl
44	NHNHSO ₂ CH ₃	0	-	1-pyrrolidinyl	Cl
45	NHNHSO ₂ CH ₃	0	-	2-thienyl	Cl
46	Structure-(j)	0	-	-OH	Cl
47	NHCH ₂ CH ₂ OCH ₃	0	<u>5-Bromo</u>	2-thienyl	Cl
48	Structure-(k)	0	-	2-thienyl	Cl
49	Structure - (l)	0	-	2-thienyl	Cl
50	-NHNHSO ₂ isopropyl	0	-	2-thienyl	Br
51	-NHNHSO ₂ CH ₃	0	-	Structure (m)	Cl
52	-NHNHSO ₂ CH ₃	0	-	Structure (n)	Cl
53	-NHNHSO ₂ CH ₃	1	5-Bromo	2-thienyl	Br
54	-NHNHCO ₂ C ₂ H ₅	0	-	2-thienyl	Br
55	-NHNHSO ₂ CH ₃	0	-	5-chloro-2-thienyl	Br
56	Structure (o)	0	-	4-nitro-2-thienyl	Cl

IN THE CLAIMS:

Claims 15, 30, 35, 40, 45, 64, 70 and 76 are canceled.

The claims are amended as follows:

1. (amended) A cosmetic composition comprising an effective amount of a compound with free radical scavenging, AGE breaking and AGE-formation inhibiting activity having the formula (I),



(I)

or its cosmetically acceptable salts contained in a cosmetically acceptable carrier

wherein

~~R₁ is -R₄-R₅ or -N(R₇) N (R₇) R₉ and Y-R₁₁;~~

~~R₄ is selected from the group consisting of -N(R₇)R₆O-,~~

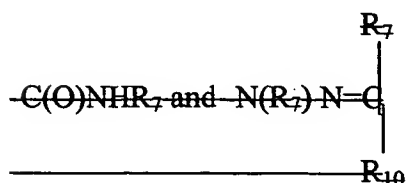
~~-N(R₇)R₆N(R₇),~~

~~-OR₆O-, and -OR₆N(R₇)-,~~

~~where R₆ is alkyl;~~

~~R₅ is selected from the group consisting of alkyl, aryl including heteroaryl, -COR₇-, -SO₂R₇-,~~

~~C(S) NHR₇-, C(NH)NHR₇-, -COR₁₀;~~



where R_7 is selected from the group consisting of H, alkyl and aryl including heteroaryl, provided R_7 may be the same or different for R_1 and R_3 in the same compound;

R_2 is selected from the group consisting of F, Cl, Br, I, OR_7 , NO_2 , alkyl, aryl including heteroaryl, formyl, acyl, $\text{C}(\text{O})\text{NR}_7\text{R}_{10}$, $\text{C}(\text{O})\text{OR}_7$, NR_7R_{10} , $\text{N}=\text{C}(\text{R}_7)(\text{R}_{10})$, SR_7 , SO_2NH_2 , SO_2 alkyl and SO_2 aryl;

m is 0, 1 or 2;

R_3 is selected from the group consisting of R_7 , OR_7 , $\text{N}(\text{R}_7)(\text{R}_{10})$, $\text{N}=\text{C}(\text{R}_7)(\text{R}_{10})$, $\text{N}(\text{R}_7)\text{N}(\text{R}_7)(\text{R}_{10})$, $\text{N}(\text{R}_7)\text{N}=\text{C}(\text{R}_7)(\text{R}_{10})$ and $\text{CH}(\text{R}_7)\text{C}(\text{O})\text{R}_8$

where R_8 is selected from the group consisting of R_7 , OR_7 and NR_7R_{10} ;

R_9 is selected from the group consisting of hydrogen, alkyl, aryl including heteroaryl, $\text{C}(\text{O})\text{R}_{10}$, SO_2R_{10} , $\text{C}(\text{S})\text{NHR}_{10}$, $\text{C}(\text{NH})\text{NH}(\text{R}_{10})$ and $\text{C}(\text{O})\text{NHR}_{10}$;

R_{10} is selected from the group consisting of H, alkyl and aryl, including heteroaryl and in each case may be the same or different from substituent R_7 , provided R_{10} may be the same or different for R_1 and R_3 in the same compound;

~~Y is selected from oxygen, NH , NR_{12} and null~~

~~R_{11} and R_{12} are independently selected from hydrogen, alkyl and aryl~~

X is selected from the group consisting of a halide ion, acetate ion, perchlorate ion, sulfonate ion, oxalate ion, citrate ion, tosylate ion, maleate ion, mesylate ion, carbonate ion, sulfite ion,

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appln. No. 09/995,731

phosphoric hydrogen ion, phosphonate ion, phosphate ion, ~~BF₄~~- BF₄⁻ and ~~PF₆~~- PF₆⁻;

with proviso that,

- (iii) when two alkyl groups are present on the same carbon or nitrogen, they may be linked together to form a cyclic structure;
- (iv) the nitrogen of heteroaryl ring of R₁₀, when present, may be quaternized;
- (iii) when R₃ is OR₇ and R₁ is -NHNH₂ then R₇ is not alkyl ~~and~~
- (iv) when R₃ is OR₇, R₁ is N(R₇)N(R₇)R₉ and R₉ is C(O)R₁₀ where R₁₀ is alkyl, then R₇ is not hydrogen,and
- (v) at least one heteroaryl group is present.

4. (amended) The composition as claimed in claim 1, wherein for ~~the~~ said compound m is 0 or 1.

5. (amended) The composition as claimed in claim 2, wherein for ~~the~~ said compound m is 0 or 1.

6. (amended) The composition as claimed in claim 3, wherein for ~~the~~ said compound m is 0 or 1.

7. (amended) The composition as claimed in claim 1, wherein for ~~the~~ said compound m is 0.

8. (amended) The composition as claimed in claim 2, wherein for ~~the~~ said compound m is 0.

9. (amended) The composition as claimed in claim 3, wherein for ~~the~~ said compound m is 0.

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

10. (amended) The composition as claimed in claim 1, wherein for the said compound X is a halide ion.

11. (amended) The composition as claimed in claim 1, wherein said compound is selected from the group consisting of:

(a) N,N'-bis[3-carbonyl-1-(2-thien-2'-yl-2-oxoethyl)-3-pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof,

(b) 1-(2-ethoxy-2-oxoethyl)-3-(2-(2-pyridyl)hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and

~~(c) 1-(2-ethoxy-2-oxoethyl)-3-(2-(benzoyloxy)ethylamino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,~~

(d) N,N'-bis[3-carbonyl-1-(2-phenyl-2-oxoethyl)pyridinium]hydrazine dibromide or other cosmetically acceptable salts thereof,

~~(e) 1-(2-phenyl-2-oxoethyl)-3-(hydrazinocarbonyl)pyridinium bromide or other cosmetically acceptable salts thereof,~~

(f) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and

(g) N,N'-bis[3-carbonyl-1-(2-(2',4'-dichlorophenyl)-2-oxoethyl) pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof,

~~(h) 1-(2-phenyl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,~~

~~(i) 1-(2-ethoxy-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or~~

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

~~other cosmetically acceptable salts thereof;~~

~~(j) 1-(2-phenyl-2-oxoethyl)-3-(phenylsulfonylhydrazino-carbonyl)pyridinium bromide or other
cosmetically acceptable salts thereof;~~

~~(k) 1-(2-phenyl-2-oxoethyl)-2-chloro-3-(phenylsulfonylhydrazino-carbonyl)pyridinium bromide
or other cosmetically acceptable salts thereof;~~

~~(l) 1-(2-thien-2'-yl-2-oxoethyl)-4-(2-(benzoyloxy)-ethylaminocarbonyl)pyridinium bromide or
other cosmetically acceptable salts thereof;~~

~~(m) 1-(2-(2,4'-dichlorophenyl)-2-oxoethyl)-3-(2-(benzoyloxy)-ethylaminocarbonyl)
pyridinium bromide or other cosmetically acceptable salts thereof;~~

~~(n) 1-(2-phenyl-2-oxoethyl)-3-(2-(acetoxy)-ethyloxy-carbonyl)pyridinium
bromide or other cosmetically acceptable salts thereof and~~

~~(o) 1-(2-ethoxy-2-oxoethyl)-3-(2-(benzoyloxy)-ethyloxy-carbonyl)pyridinium
bromide or other cosmetically acceptable salts thereof.~~

12. (amended) The composition as claimed in claim 1, wherein said compound is selected
from the group consisting of:

~~(p) 1-(2-phenylamino-2-oxoethyl)-4-(phenylsulfonylhydrazino-carbonyl)pyridinium chloride or
other cosmetically acceptable salts thereof;~~

~~(q) 1-(2-(2,4'-dichlorophenyl)-2-oxoethyl)-3-(2(methoxy)-ethyloxy-carbonyl)pyridinium
bromide or other cosmetically acceptable salts thereof;~~

~~(r) 1-(2-phenylamino-2-oxoethyl)-3-((benzoyloxy)-ethylaminocarbonyl)pyridinium chloride or
other cosmetically acceptable salts thereof;~~

(s) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylaminocarbonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and

~~(t) 1-(2-phenyl-2-oxoethyl)-3-(2-(acetoxy)-ethylaminocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,~~

~~(u) 1-(2-phenylamino-2-oxoethyl)-3-(phenyl sulfonyl hydrazino-carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,~~

~~(v) 1-(2-phenylamino-2-oxoethyl)-3-((4-methylphenyl)sulfonyl hydrazinocarbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,~~

~~(w) 1-(2-phenyl-2-oxoethyl)-3-(2-(benzoyloxy)ethyloxy-carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,~~

(x) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylcarbonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

~~(y) 1-(2-ethoxy-2-oxoethyl)-3-((phenylmethyl)sulfonyl hydrazino-carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof and~~

~~(z) 1-(2-phenyl-2-oxoethyl)-3-((phenylmethyl)sulfonyl hydrazino-carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof.~~

13. (amended) The composition as claimed in claim 1, wherein said compound is selected from the group consisting of :

(aa) N, N' - bis [3-carbonyl-1-(2-furan-2'-yl-2-oxoethyl) pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof,

(ab) N,N'-bis [3-carbonyl -1- (2-thien-2'-yl-2-oxoethyl) pyridinium] hydrazine dichloride or

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appln. No. 09/995,731

other cosmetically acceptable salts thereof,

(ac) N,N'-bis-[3-carbonyl-1-(2-cyclopropylamino-2-oxoethyl) pyridinium] hydrazine dichloride
or other cosmetically acceptable salts thereof,

~~(ad) 1-(2',4'-dichlorophenyl-2-oxoethyl)-3-(2-methoxyethyl aminocarbonyl)-pyridinium bromide
or other cosmetically acceptable salts thereof,~~

~~(ae) 1-(2-thien-2'-yl-2-oxoethyl)-3-((2-methoxyethyl) amino carbonyl)-5-bromo pyridinium
chloride or other cosmetically acceptable salts thereof,~~

(af) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or
other cosmetically acceptable salts thereof,

(ag) 1-(2-thien-2'-yl-2-oxoethyl)-3-(2-(2-chloro-3-pyridoylhydrazinocarbonyl) -pyridinium
chloride or other cosmetically acceptable salts thereof, and

~~(ah) 1-(2-cyclopropylamino-2-oxoethyl)-3-(2-methoxyethylaminocarbonyl)-pyridinium chloride
or other cosmetically acceptable salts thereof,~~

~~(ai) 1-(2-isopropylamino-2-oxoethyl)-3-(2-methylsulfonylhydrazinocarbonyl)-pyridinium
chloride or other cosmetically acceptable salts thereof,~~

~~(aj) 1-(2-phenylamino-2-oxo-ethyl)-3-({2-(1-oxo-3-cyclohexyl)-ethyl}-hydrazinocarbonyl)-
pyridinium bromide or other cosmetically acceptable salts thereof,~~

(ak) 1-(2-thien-2'-yl-2-oxoethyl)-3-[2-(benzoyloxy)ethylamino carbonyl] pyridinium bromide or
other cosmetically acceptable salts thereof,

(al) 1-(4-ethoxy-2,4-dioxobutyl)-3-(2-(benzoxylloxy)ethylamino carbonyl) pyridinium chloride
or other cosmetically acceptable salts thereof and

(am) 1-(2-thien-2'-yl-2-oxoethyl)-3-[1-oxo-1-(2-methoxy carbonyl) pyridyl] hydrazino pyridinium chloride or other cosmetically acceptable salts thereof.

14. (amended) The composition as claimed in claim 1, wherein said compound is selected from the group consisting of:

(an) 1-[1-(2-thien-2'-yl-2-oxoethyl)-5-aminocarbonyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(ao) 1-(2-thien-2'-yl-2-oxoethyl)-3-(trifluoromethanesulfonyl hydrazino carbonyl) - pyridinium bromide or other cosmetically acceptable salts thereof,

(ap) 1-[1-(2-thien-2'-yl-2-oxoethyl)-6-methyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(aq) N,N'-bis[3-carbonyl-1-(2-(5-methyl-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(ar) N,N'-bis[3-carbonyl-1-(2-(5-chloro-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(as) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-6-methyl pyridinium bromide or other cosmetically acceptable salts thereof,

(at) N,N'-bis[3-carbonyl-1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(au) 1-(2-phenylamino-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium chloride or other

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

~~cosmetically acceptable salts thereof,~~

(av) 1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(aw) 1-(2-(5-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,

(ax) 1-(2-(5-chloro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(ay) 1-(2-thien-2'-yl-2-oxoethyl)-3-(ethoxycarbonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(az) 1-(2-thien-2'-yl-2-oxoethyl)-3-(isopropylsulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(ba) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-5-bromo pyridinium bromide or other cosmetically acceptable salts thereof,

~~(bb) 1-(2-(2-ethoxy carbonyl pyrrolidin-1-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,~~

(bc) 1-(2-(5-methyl-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,

~~(bd) 1-(2-(4-carboethoxy thiazolidin-3-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,~~

~~(be) 1-(2-(4-benzyl piperidin-1-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,~~

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

(bf) N,N' (-bis[3-carbonyl-1-(2-(2-ethoxycarbonyl pyrrolidin-1-yl)-2-oxoethyl) pyridinium]
hydrazine dichloride or other cosmetically acceptable salts thereof,

~~(bg) 1-(2-phenylamino-2-oxoethyl)-4-[2-(benzoyloxy)-ethylamino-carbonyl]-pyridinium
chloride or other cosmetically acceptable salts thereof,~~

(bh) 1-(2-thien-2(-yl)-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other
cosmetically acceptable salts thereof, and

(bi) 1-(2-thien-2(-yl)-2-oxoethyl)-3-(p-methoxy phenyl sulfonyl hydrazino carbonyl) pyridinium
bromide or other cosmetically acceptable salts thereof,

~~(bj) 1-(2-ethoxy-2-oxoethyl)-3-(phenyl aminocarbonyl-hydrazino-carbonyl)-pyridinium
bromide or other cosmetically acceptable salts thereof,~~

~~(bk) 1-(2-ethoxy-2-oxoethyl)-3-(p-toluene-sulfonyl hydrazino-carbonyl)-pyridinium bromide or
other cosmetically acceptable salts thereof,~~

~~(bl) 1-(2-phenyl-2-oxoethyl)-3-(phenylamino-carbonyl-hydrazino-carbonyl)-pyridinium bromide
or other cosmetically acceptable salts thereof,~~

~~(bm) 1-(2-phenylamino-2-oxoethyl)-3-(benzyl-sulfonyl hydrazino-carbonyl)-pyridinium chloride
or other cosmetically acceptable salts thereof,~~

~~(bn) 1-(2-phenyl-2-oxoethyl)-4-(methanesulfonyl hydrazino-carbonyl)-pyridinium bromide or
other cosmetically acceptable salts thereof,~~

~~(bo) 1-(2-phenyl-2-oxoethyl)-3-(phenyl hydrazino-carbonyl)-pyridinium bromide
or other cosmetically acceptable salts thereof,~~

~~(bp) 1-(2-ethoxy-2-oxoethyl)-4-[2-(benzoyloxy)-ethyl-amino-carbonyl]-pyridinium bromide or~~

~~other cosmetically acceptable salts thereof,~~

~~(bq) 1-(2-ethoxy-2-oxoethyl)-3-(phenylhydrazino-carbonyl)-pyridinium bromide or other
cosmetically acceptable salts thereof,~~

~~(br) 1-(2-phenyl-2-oxoethyl)-3-(p-methoxyphenyl-sulfonyl-hydrazino-carbonyl)-pyridinium
bromide or other cosmetically acceptable salts thereof,~~

~~(bs) 1-(2-phenyl-2-oxoethyl)-4-[2-(benzoyloxy)-ethyl-amino-carbonyl]-pyridinium bromide or
other cosmetically acceptable salts thereof and~~

~~(bt) 1-(2-ethoxy-2-oxoethyl)-4-(p-methanesulfonyl-hydrazino-carbonyl)-pyridinium bromide
or other cosmetically acceptable salts thereof.~~

17. (amended) A composition useful for the cosmetic application comprising an effective amount of a said compound with free radical scavenger, AGE breaker and AGE formation inhibitor activity as defined in claim 1 or its cosmetically acceptable salts contained in a cosmetically acceptable carrier wherein said composition is effective for ~~atleast~~ at least one of the following applications:

- a) reversal and prevention of wrinkles,
- b) reversal and prevention of fine lines,
- c) promotion of epidermal growth,
- d) photo protection of skin,
- e) reversal and prevention of skin discoloration,
- f) reversal and prevention of age spots,
- g) conditioning and prevention of dry spot,

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

- h) reversal and prevention of stretch marks,
- i) reversal and prevention of blemishes,
- j) skin care and conditioning,
- h) reversal and prevention of senile xerosis,
- l) conditioning and prevention of sun burns,
- m) preventing and reversing the loss of collagen,
- n) improving skin texture,
- o) improving skin tone,
- p) enhancing of skin thickness,
- q) decreasing pore size,
- r) restoring skin luster,
- s) minimising signs of fatigue,
- t) reducing acne,
- w) treatment of Telangiectasia and
- v) improving aesthetic appearance of hair and nails.

19. (amended) A method of cosmetic application with reversing and preventing effects on aging and wrinkling of the skin comprising applying an effective amount of a cosmetic composition comprising a said compound with free radical scavenger, AGE-breaker and AGE formation-inhibitor activity having the formula (I) as defined in Claim 1 or its cosmetically acceptable salts contained in a cosmetically acceptable carrier.

23. (amended) A method of cosmetic application with reversing and preventing effects on

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

~~atleast~~ at least one of the following :

- i) fine lines,
- ii) skin discoloration
- iii) age spots
- iv) stretch marks
- v) blemishes and
- vi) senile xerosis
- vii) preventing and reversing loss of collagen

comprising applying an effective amount of a cosmetic composition comprising said compound with free radical scavenger, AGE breaker and AGE formation inhibitor activity having the formula (I) as defined in claim 1 or its cosmetically acceptable salts contained in a cosmetically acceptable carrier.

24. (amended) A method of cosmetic application with conditioning and preventing effects in skin dryness and /or sun burns comprising applying an effective amount of a cosmetic composition comprising a said compound with free radical scavenger, AGE breaker and AGE formation inhibitor activity having the formula (I) as defined in claim 1 or cosmetically acceptable salts thereof contained in a cosmetically acceptable carrier.

25. (amended) A method of cosmetic application with effects of promoting epidermal growth and/or photo protection, improving skin texture, improving skin tone, enhancing skin thickness, decreasing pore size, restoring skin luster, minimizing signs of fatigue, reducing tone, treatment of telangiectasia comprising applying an effective amount of a cosmetic composition

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

comprising a said compound with free radical scavenger, AGE breaker and AGE formation inhibitor activity having the formula (I) as defined in claim 1 or its cosmetically acceptable salts contained in a cosmetically acceptable carrier.

26. (amended) The method as claimed in claim 19, wherein said compound is selected from the group consisting of the following compounds:

(a) N,N'-bis[3-carbonyl-1-(2-thien -2'- yl -2-oxoethyl) -3-pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof,

(b) 1-(2-ethoxy -2-oxoethyl) -3-(2-(2-pyridyl)hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

~~(c) 1-(2-ethoxy -2-oxoethyl) -3-(2-(benzoyloxy)-ethylamino-carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,~~

(d) N,N'-bis[3-carbonyl-1-(2-phenyl-2-oxoethyl)pyridinium]hydrazine dibromide or other cosmetically acceptable salts thereof,

~~(e) 1-(2-phenyl-2-oxoethyl) -3-(hydrazinocarbonyl)pyridinium bromide or other cosmetically acceptable salts thereof,~~

(f) 1-(2-thien -2'-yl -2-oxoethyl) -3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and

(g) N,N'-bis[3-carbonyl-1-(2-(2',4'-dichlorophenyl)-2-oxoethyl) pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof,

~~(h) 1-(2-phenyl-2-oxoethyl) -3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,~~

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

~~(i) 1-(2-ethoxy-2-oxoethyl)-3-(methanesulfonylhydrazinocarbonyl)pyridinium bromide or other cosmetically acceptable salts thereof,~~

~~(j) 1-(2-phenyl-2-oxoethyl)-3-(phenylsulfonylhydrazino-carbonyl)pyridinium bromide or other cosmetically acceptable salts thereof,~~

~~(k) 1-(2-phenyl-2-oxoethyl)-2-chloro-3-(phenylsulfonylhydrazino-carbonyl)pyridinium bromide or other cosmetically acceptable salts thereof,~~

~~(l) 1-(2-thien-2'-yl-2-oxoethyl)-4-(2-(benzoyloxy)-ethylaminocarbonyl)pyridinium bromide or other cosmetically acceptable salts thereof,~~

~~(m) 1-(2-(2,4'-dichlorophenyl)-2-oxoethyl)-3-(2-(benzoyloxy)-ethylaminocarbonyl)pyridinium bromide or other cosmetically acceptable salts thereof,~~

~~(n) 1-(2-phenyl-2-oxoethyl)-3-(2-(acetoxy)-ethyloxy-carbonyl)pyridinium bromide or other cosmetically acceptable salts thereof and~~

~~(o) 1-(2-ethoxy-2-oxoethyl)-3-(2-(benzoyloxy)-ethyloxy-carbonyl)pyridinium bromide or other cosmetically acceptable salts thereof.~~

27. (amended) The method as claimed in claim 19, wherein said compound is selected from the group consisting of the following compounds:

~~(p) 1-(2-phenylamino-2-oxoethyl)-4-(phenylsulfonylhydrazino-carbonyl)pyridinium chloride or other cosmetically acceptable salts thereof,~~

~~(q) 1-(2-(2,4'-dichlorophenyl)-2-oxoethyl)-3-(2(methoxy)-ethyloxy-carbonyl)pyridinium bromide or other cosmetically acceptable salts thereof,~~

~~(r) 1-(2-phenylamino-2-oxoethyl)-3-((benzoyloxy)-ethylaminocarbonyl)pyridinium chloride or~~

~~other cosmetically acceptable salts thereof,~~

(s) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylaminocarbonyl hydrazinocarbonyl) pyridinium
bromide or other cosmetically acceptable salts thereof, and

~~(t) 1-(2-phenyl-2-oxoethyl)-3-(2-(acetoxymethyl)aminocarbonyl) pyridinium bromide or other
cosmetically acceptable salts thereof,~~

~~(u) 1-(2-phenylamino-2-oxoethyl)-3-(phenylsulfonylhydrazinocarbonyl) pyridinium chloride
or other cosmetically acceptable salts thereof,~~

~~(v) 1-(2-phenylamino-2-oxoethyl)-3-((4-methylphenyl)sulfonylhydrazinocarbonyl) pyridinium
chloride or other cosmetically acceptable salts thereof,~~

~~(w) 1-(2-phenyl-2-oxoethyl)-3-(2-(benzoyloxy)ethoxycarbonyl) pyridinium bromide or other
cosmetically acceptable salts thereof,~~

(x) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylcarbonyl hydrazino carbonyl) pyridinium bromide or
other cosmetically acceptable salts thereof,

(y) 1-(2-ethoxy-2-oxoethyl)-3-((phenylmethyl)sulfonylhydrazino carbonyl)pyridinium bromide
or other cosmetically acceptable salts thereof and

~~(z) 1-(2-phenyl-2-oxoethyl)-3-((phenylmethyl)sulfonylhydrazino carbonyl)pyridinium bromide
or other cosmetically acceptable salts thereof.~~

28. (amended) The method as claimed in claim 19, wherein said compound is selected from
the group consisting of the following compounds:

(aa) N, N' - bis [3-carbonyl-1-(2-furan-2'-yl-2-oxoethyl) pyridinium] hydrazine dibromide or
other cosmetically acceptable salts thereof,

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

(ab) N,N'-bis [3-carbonyl -1- (2-thien-2'-yl-2-oxoethyl) pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(ac) N,N'-bis-[3-carbonyl-1-(2-cyclopropylamino-2-oxoethyl) pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

~~(ad) 1-(2',4'-dichlorophenyl-2-oxoethyl)-3-(2-methoxyethyl-aminocarbonyl)-pyridinium bromide or other cosmetically acceptable salts thereof,~~

~~(ae) 1-(2-thien-2'-yl-2-oxoethyl)-3-((2-methoxyethyl)-amino-carbonyl)-5-bromo-pyridinium chloride or other cosmetically acceptable salts thereof,~~

(af) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,

(ag) 1-(2-thien-2'-yl-2-oxoethyl)-3-(2-(2-chloro-3-pyridoylhydrazinocarbonyl) -pyridinium chloride or other cosmetically acceptable salts thereof, and

~~(ah) 1-(2-cyclopropylamino-2-oxoethyl)-3-(2-methoxyethylaminocarbonyl)-pyridinium chloride or other cosmetically acceptable salts thereof,~~

~~(ai) 1-(2-isopropylamino-2-oxoethyl)-3-(2-methylsulfonylhydrazinocarbonyl)-pyridinium chloride or other cosmetically acceptable salts thereof,~~

~~(aj) 1-(2-phenylamino-2-oxo-ethyl)-3-({2-(1-oxo-3-cyclohexyl)-ethyl}-hydrazinocarbonyl)-pyridinium bromide or other cosmetically acceptable salts thereof,~~

~~(ak) 1-(2-thien-2'-yl-2-oxoethyl)-3-[2-(benzoyloxy)ethylamino-carbonyl]-pyridinium bromide or other cosmetically acceptable salts thereof,~~

(al) 1-(4-ethoxy-2,4-dioxobutyl)-3-(2-(benzoxyl-oxy)ethylamino-carbonyl)-pyridinium chloride

~~or other cosmetically acceptable salts thereof and~~

(am) 1-(2-thien-2'-yl-2-oxoethyl)-3-[1-oxo-1-(2-methoxy carbonyl) pyridyl] hydrazino
pyridinium chloride or other cosmetically acceptable salts thereof.

29. (amended) The method as claimed in claim 19, wherein said compound is selected from
the group consisting of the following compounds:

(an) 1-[1-(2-thien-2'-yl-2-oxoethyl)-5-aminocarbonyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-
yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other cosmetically acceptable
salts thereof,

(ao) 1-(2-thien-2'-yl-2-oxoethyl)-3-(trifluoromethanesulfonyl hydrazino carbonyl) - pyridinium
bromide or other cosmetically acceptable salts thereof,

(ap) 1-[1-(2-thien-2'-yl-2-oxoethyl)-6-methyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-
oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other cosmetically acceptable salts
thereof,

(aq) N,N'-bis[3-carbonyl-1-(2-(5-methyl-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine
dichloride or other cosmetically acceptable salts thereof,

(ar) N,N'-bis[3-carbonyl-1-(2-(5-chloro-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine
dichloride or other cosmetically acceptable salts thereof,

(as) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-6-methyl pyridinium
bromide or other cosmetically acceptable salts thereof,

(at) N,N'-bis[3-carbonyl-1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)pyridinium] hydrazine dichloride
or other cosmetically acceptable salts thereof,

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

~~(au) 1-(2-phenylamino-2-oxoethyl)-3-(phenylhydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,~~

(av) 1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(aw) 1-(2-(5-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,

(ax) 1-(2-(5-chloro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(ay) 1-(2-thien-2'-yl-2-oxoethyl)-3-(ethoxycarbonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(az) 1-(2-thien-2'-yl-2-oxoethyl)-3-(isopropylsulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(ba) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-5-bromo pyridinium bromide or other cosmetically acceptable salts thereof,

~~(bb) 1-(2-(2-ethoxy carbonyl pyrrolidin-1-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,~~

(bc) 1-(2-(5-methyl-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,

~~(bd) 1-(2-(4-carboethoxy thiazolidin-3-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,~~

(be) 1-(2-(4-benzyl piperidin-1-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

~~pyridinium chloride or other cosmetically acceptable salts thereof,~~

(bf) N,N' (-bis[3-carbonyl-1-(2-(2-ethoxycarbonyl pyrrolidin-1-yl)-2-oxoethyl) pyridinium]

hydrazine dichloride or other cosmetically acceptable salts thereof,

(bg) ~~1-(2-phenylamino-2-oxoethyl)-4-[2-(benzoyloxy)-ethylamino-carbonyl]-pyridinium~~

~~chloride or other cosmetically acceptable salts thereof,~~

(bh) 1-(2-thien-2(-yl-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other
cosmetically acceptable salts thereof, and

(bi) 1-(2-thien-2(-yl-2-oxoethyl)-3-(p-methoxy phenyl sulfonyl hydrazino carbonyl) pyridinium
bromide or other cosmetically acceptable salts thereof,

(bj) ~~1-(2-ethoxy-2-oxoethyl)-3-(phenyl aminocarbonyl-hydrazino-carbonyl)-pyridinium~~
~~bromide or other cosmetically acceptable salts thereof,~~

(bk) ~~1-(2-ethoxy-2-oxoethyl)-3-(p-toluene sulfonyl hydrazino-carbonyl)-pyridinium bromide or~~
~~other cosmetically acceptable salts thereof,~~

(bl) ~~1-(2-phenyl-2-oxoethyl)-3-(phenylamino-carbonyl-hydrazino-carbonyl)-pyridinium bromide~~
~~or other cosmetically acceptable salts thereof,~~

(bm) ~~1-(2-phenylamino-2-oxoethyl)-3-(benzyl sulfonyl hydrazino-carbonyl)-pyridinium chloride~~
~~or other cosmetically acceptable salts thereof,~~

(bn) ~~1-(2-phenyl-2-oxoethyl)-4-(methanesulfonyl hydrazino-carbonyl)-pyridinium bromide or~~
~~other cosmetically acceptable salts thereof,~~

(bo) ~~1-(2-phenyl-2-oxoethyl)-3-(phenyl hydrazino-carbonyl)-pyridinium bromide or other~~
~~cosmetically acceptable salts thereof,~~

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

~~(bp) 1-(2-ethoxy-2-oxoethyl)-4-[2-(benzoyloxy)-ethyl-amino-carbonyl]-pyridinium bromide or other cosmetically acceptable salts thereof;~~

~~(bq) 1-(2-ethoxy-2-oxoethyl)-3-(phenyl-hydrazino-carbonyl)-pyridinium bromide or other cosmetically acceptable salts thereof;~~

~~(br) 1-(2-phenyl-2-oxoethyl)-3-(p-methoxyphenyl-sulfonyl-hydrazino-carbonyl)-pyridinium bromide or other cosmetically acceptable salts thereof;~~

~~(bs) 1-(2-phenyl-2-oxoethyl)-4-[2-(benzoyloxy)-ethyl-amino-carbonyl]-pyridinium bromide or other cosmetically acceptable salts thereof and~~

(bt) 1-(2-ethoxy-2-oxoethyl)-4-(p-methanesulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof.

31. (amended) The method as claimed in claim 23, wherein said compound is selected from the group consisting of the following compounds:

(a) N,N'-bis[3-carbonyl-1-(2-thien-2'-yl-2-oxoethyl)-3-pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof,

(b) 1-(2-ethoxy-2-oxoethyl)-3-(2-(2-pyridyl)hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

~~(c) 1-(2-ethoxy-2-oxoethyl)-3-(2-(benzoyloxy)-ethylamino-carbonyl)-pyridinium bromide or other cosmetically acceptable salts thereof;~~

(d) N,N'-bis[3-carbonyl-1-(2-phenyl-2-oxoethyl)pyridinium]hydrazine dibromide or other cosmetically acceptable salts thereof,

~~(e) 1-(2-phenyl-2-oxoethyl)-3-(hydrazinocarbonyl)pyridinium bromide or other cosmetically~~

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

~~acceptable salts thereof,~~

(f) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and

(g) N,N'-bis[3-carbonyl-1-(2-(2',4'-dichlorophenyl)-2-oxoethyl) pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof; .

~~(h) 1-(2-phenyl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,~~

~~(i) 1-(2-ethoxy-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,~~

~~(j) 1-(2-phenyl-2-oxoethyl)-3-(phenylsulfonylhydrazino-carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,~~

~~(k) 1-(2-phenyl-2-oxoethyl)-2-chloro-3-(phenylsulfonyl hydrazino-carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,~~

~~(l) 1-(2-thien-2'-yl-2-oxoethyl)-4-(2-(benzoyloxy)-ethyl aminocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,~~

~~(m) 1-(2-(2',4'-dichlorophenyl)-2-oxoethyl)-3-(2-(benzoyloxy)-ethylaminocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,~~

~~(n) 1-(2-phenyl-2-oxoethyl)-3-(2-(acetoxy)-ethyloxy-carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof and~~

~~(o) 1-(2-ethoxy-2-oxoethyl)-3-(2-(benzoyloxy)-ethyloxy-carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof~~

32. (amended) The method as claimed in claim 23, wherein said compound is selected from the group consisting of the following compounds:

~~(p) 1-(2-phenylamino-2-oxoethyl)-4-(phenylsulfonylhydrazino-carbonyl)pyridinium chloride or other cosmetically acceptable salts thereof;~~

~~(q) 1-(2-(2,4'-dichlorophenyl)-2-oxoethyl)-3-(2(methoxy)-ethyloxy-carbonyl)pyridinium bromide or other cosmetically acceptable salts thereof;~~

~~(r) 1-(2-phenylamino-2-oxoethyl)-3-((benzoyloxy)-ethylaminocarbonyl)pyridinium chloride or other cosmetically acceptable salts thereof;~~

(s) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylaminocarbonylhydrazinocarbonyl)pyridinium bromide or other cosmetically acceptable salts thereof, and

~~(t) 1-(2-phenyl-2-oxoethyl)-3-(2-(acetoxy)-ethylaminocarbonyl)pyridinium bromide or other cosmetically acceptable salts thereof;~~

~~(u) 1-(2-phenylamino-2-oxoethyl)-3-(phenylsulfonylhydrazino-carbonyl)pyridinium chloride or other cosmetically acceptable salts thereof;~~

~~(v) 1-(2-phenylamino-2-oxoethyl)-3-((4-methylphenyl)sulfonylhydrazinocarbonyl)pyridinium chloride or other cosmetically acceptable salts thereof;~~

~~(w) 1-(2-phenyl-2-oxoethyl)-3-(2-(benzoyloxy)ethyloxy-carbonyl)pyridinium bromide or other cosmetically acceptable salts thereof;~~

(x) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylcarbonylhydrazino carbonyl)
pyridinium bromide or other cosmetically acceptable salts thereof;

(y) 1-(2-ethoxy-2-oxoethyl)-3-((phenylmethyl)sulfonylhydrazino-carbonyl)pyridinium bromide

~~or other cosmetically acceptable salts thereof and~~

~~(z) 1-(2-phenyl-2-oxoethyl)-3-((phenylmethyl)sulfonylhydrazino-carbonyl)pyridinium bromide
or other cosmetically acceptable salts thereof.~~

33. (amended) The method as claimed in claim 23, wherein said compound is selected from the group consisting of the following compounds:

(aa) N, N' - bis [3-carbonyl-1-(2-furan-2'-yl-2-oxoethyl) pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof,

(ab) N,N'-bis [3-carbonyl-1-(2-thien-2'-yl-2-oxoethyl) pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(ac) N,N'-bis-[3-carbonyl-1-(2-cyclopropylamino-2-oxoethyl) pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

~~(ad) 1-(2',4'-dichlorophenyl-2-oxoethyl)-3-(2-methoxyethylaminocarbonyl)pyridinium bromide
or other cosmetically acceptable salts thereof,~~

~~(ae) 1-(2-thien-2'-yl-2-oxoethyl)-3-((2-methoxyethyl)amino-carbonyl)-5-bromo-pyridinium
chloride or other cosmetically acceptable salts thereof,~~

(af) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonylhydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,

(ag) 1-(2-thien-2'-yl-2-oxoethyl)-3-(2-(2-chloro-3-pyridoylhydrazinocarbonyl) -pyridinium chloride or other cosmetically acceptable salts thereof, and

~~(ah) 1-(2-cyclopropylamino-2-oxoethyl)-3-(2-methoxyethylaminocarbonyl)
-pyridinium chloride or other cosmetically acceptable salts thereof,~~

~~(ai) 1-(2-isopropylamino-2-oxoethyl)-3-(2-methylsulfonylhydrazinocarbonyl)-pyridinium chloride or other cosmetically acceptable salts thereof;~~

~~(aj) 1-(2-phenylamino-2-oxoethyl)-3-((2-(1-oxo-3-cyclohexyl)ethyl)-hydrazinocarbonyl)-pyridinium bromide or other cosmetically acceptable salts thereof;~~

~~(ak) 1-(2-thien-2'-yl-2-oxoethyl)-3-[2-(benzoyloxy)ethylamino-carbonyl]-pyridinium bromide or other cosmetically acceptable salts thereof;~~

~~(al) 1-(4-ethoxy-2,4-dioxobutyl)-3-(2-(benzoyloxy)ethylamino-carbonyl)-pyridinium chloride or other cosmetically acceptable salts thereof and~~

(am) 1-(2-thien-2'-yl-2-oxoethyl)-3-[1-oxo-1-(2-methoxy carbonyl) pyridyl] hydrazino pyridinium chloride or other cosmetically acceptable salts thereof.

34. (amended) The method as claimed in claim 23, wherein said compound is selected from the group consisting of the following compounds:

(an) 1-[1-(2-thien-2'-yl-2-oxoethyl)-5-aminocarbonyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(ao) 1-(2-thien-2'-yl-2-oxoethyl)-3-(trifluoromethanesulfonyl hydrazino carbonyl) - pyridinium bromide or other cosmetically acceptable salts thereof,

(ap) 1-[1-(2-thien-2'-yl-2-oxoethyl)-6-methyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(aq) N,N'-bis[3-carbonyl-1-(2-(5-methyl-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine

dichloride or other cosmetically acceptable salts thereof,

(ar) N,N'-bis[3-carbonyl-1-(2-(5-chloro-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine

dichloride or other cosmetically acceptable salts thereof,

(as) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-6-methyl pyridinium

bromide or other cosmetically acceptable salts thereof,

(at) N,N'-bis[3-carbonyl-1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)pyridinium] hydrazine dichloride
or other cosmetically acceptable salts thereof,

~~(au) 1-(2-phenylamino-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium chloride or other
cosmetically acceptable salts thereof,~~

(av) 1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium
bromide or other cosmetically acceptable salts thereof,

(aw) 1-(2-(5-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium
chloride or other cosmetically acceptable salts thereof,

(ax) 1-(2-(5-chloro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium
bromide or other cosmetically acceptable salts thereof,

(ay) 1-(2-thien-2'-yl-2-oxoethyl)-3-(ethoxycarbonyl hydrazino carbonyl) pyridinium bromide or
other cosmetically acceptable salts thereof,

(az) 1-(2-thien-2'-yl-2-oxoethyl)-3-(isopropylsulfonyl hydrazino carbonyl) pyridinium bromide
or other cosmetically acceptable salts thereof,

(ba) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-5-bromo pyridinium
bromide or other cosmetically acceptable salts thereof,

AMENDMENT UNDER 37 C.F.R. § 1.111

U.S. Appln. No. 09/995,731

~~(bb) 1-(2-(2-ethoxy carbonyl pyrrolidin-1-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)pyridinium chloride or other cosmetically acceptable salts thereof;~~

(bc) 1-(2-(5-methyl-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,

~~(bd) 1-(2-(4-carboethoxy-thiazolidin-3-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)pyridinium chloride or other cosmetically acceptable salts thereof;~~

~~(be) 1-(2-(4-benzyl piperidin-1-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)pyridinium chloride or other cosmetically acceptable salts thereof;~~

(bf) N,N'-(bis[3-carbonyl-1-(2-(2-ethoxycarbonyl pyrrolidin-1-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

~~(bg) 1-(2-phenylamino-2-oxoethyl)-4-[2-(benzoyloxy)ethylamino carbonyl]pyridinium chloride or other cosmetically acceptable salts thereof;~~

(bh) 1-(2-thien-2(-yl)-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and

(bi) 1-(2-thien-2(-yl)-2-oxoethyl)-3-(p-methoxy phenyl sulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, ;

~~(bj) 1-(2-ethoxy-2-oxoethyl)-3-(phenyl aminocarbonyl hydrazino carbonyl)pyridinium bromide or other cosmetically acceptable salts thereof;~~

~~(bk) 1-(2-ethoxy-2-oxoethyl)-3-(p-toluene-sulfonyl hydrazino carbonyl)pyridinium bromide or other cosmetically acceptable salts thereof;~~

~~(bl) 1-(2-phenyl-2-oxoethyl)-3-(phenylamino carbonyl hydrazino carbonyl)pyridinium bromide~~

~~or other cosmetically acceptable salts thereof,~~

~~(bm) 1-(2-phenylamino-2-oxoethyl)-3-(benzyl sulfonyl hydrazino carbonyl) pyridinium chloride~~
~~or other cosmetically acceptable salts thereof,~~

~~(bn) 1-(2-phenyl-2-oxoethyl)-4-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or~~
~~other cosmetically acceptable salts thereof,~~

~~(bo) 1-(2-phenyl-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other~~
~~cosmetically acceptable salts thereof,~~

~~(bp) 1-(2-ethoxy-2-oxoethyl)-4-[2-(benzoyloxy) ethyl amino carbonyl] pyridinium bromide or~~
~~other cosmetically acceptable salts thereof,~~

~~(bq) 1-(2-ethoxy-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other~~
~~cosmetically acceptable salts thereof,~~

~~(br) 1-(2-phenyl-2-oxoethyl)-3-(p-methoxyphenyl sulfonyl hydrazino carbonyl) pyridinium~~
~~bromide or other cosmetically acceptable salts thereof,~~

~~(bs) 1-(2-phenyl-2-oxoethyl)-4-[2-(benzoyloxy) ethyl amino carbonyl] pyridinium~~
~~bromide or other cosmetically acceptable salts thereof and~~

~~(bt) 1-(2-ethoxy-2-oxoethyl)-4-(p-methanesulfonyl hydrazino carbonyl) pyridinium bromide~~
~~or other cosmetically acceptable salts thereof~~

36. (amended) The method as claimed in claim 24, wherein said compound is selected from the group consisting of the following compounds:

(a) N,N'-bis[3-carbonyl-1-(2-thien-2'-yl-2-oxoethyl)-3-pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof,

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

(b) 1-(2-ethoxy-2-oxoethyl)-3-(2-(2-pyridyl)hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

~~(c) 1-(2-ethoxy-2-oxoethyl)-3-(2-(benzoyloxy)ethylamino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,~~

(d) N,N'-bis[3-carbonyl-1-(2-phenyl-2-oxoethyl)pyridinium]hydrazine dibromide or other cosmetically acceptable salts thereof,

~~(e) 1-(2-phenyl-2-oxoethyl)-3-(hydrazinocarbonyl)pyridinium bromide or other cosmetically acceptable salts thereof,~~

(f) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and

(g) N,N'-bis[3-carbonyl-1-(2-(2',4'-dichlorophenyl)-2-oxoethyl) pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof, .

~~(h) 1-(2-phenyl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,~~

~~(i) 1-(2-ethoxy-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,~~

~~(j) 1-(2-phenyl-2-oxoethyl)-3-(phenylsulfonylhydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,~~

~~(k) 1-(2-phenyl-2-oxoethyl)-2-chloro-3-(phenylsulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,~~

~~(l) 1-(2-thien-2'-yl-2-oxoethyl)-4-(2-(benzoyloxy)ethyl aminocarbonyl) pyridinium bromide or~~

~~other cosmetically acceptable salts thereof,~~

~~(m) 1-(2-(2,4'-dichlorophenyl)-2-oxoethyl)-3-(2-(benzoyloxy)ethylaminocarbonyl)~~

~~pyridinium bromide or other cosmetically acceptable salts thereof,~~

~~(n) 1-(2-phenyl-2-oxoethyl)-3-(2-(acetoxyl)ethyloxy carbonyl) pyridinium bromide or other
cosmetically acceptable salts thereof and~~

~~(o) 1-(2-ethoxy-2-oxoethyl)-3-(2-(benzoyloxy)ethyloxy carbonyl) pyridinium bromide or other
cosmetically acceptable salts thereof~~

37. (amended) The method as claimed in claim 24, wherein said compound is selected from
the group consisting of the following compounds:

~~(p) 1-(2-phenylamino-2-oxoethyl)-4-(phenylsulfonylhydrazino carbonyl)pyridinium chloride or
other cosmetically acceptable salts thereof,~~

~~(q) 1-(2-(2,4'-dichlorophenyl)-2-oxoethyl)-3-(2(methoxy)ethyloxy carbonyl) pyridinium
bromide or other cosmetically acceptable salts thereof,~~

~~(r) 1-(2-phenylamino-2-oxoethyl)-3-((benzoyloxy)ethylaminocarbonyl) pyridinium chloride or
other cosmetically acceptable salts thereof,~~

(s) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylaminocarbonyl hydrazinocarbonyl) pyridinium
bromide or other cosmetically acceptable salts thereof, and

~~(t) 1-(2-phenyl-2-oxoethyl)-3-(2-(acetoxyl)ethylaminocarbonyl) pyridinium bromide or other
cosmetically acceptable salts thereof,~~

~~(u) 1-(2-phenylamino-2-oxoethyl)-3-(phenylsulfonylhydrazino carbonyl) pyridinium chloride
or other cosmetically acceptable salts thereof,~~

~~(v) 1-(2-phenylamino-2-oxoethyl)-3-((4-methylphenyl)sulfonylhydrazinocarbonyl)~~

~~pyridinium chloride or other cosmetically acceptable salts thereof,~~

~~(w) 1-(2-phenyl-2-oxoethyl)-3-(2-(benzoyloxy)ethyloxy carbonyl)pyridinium bromide or other~~

~~cosmetically acceptable salts thereof,~~

(x) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylcarbonylhydrazino carbonyl)pyridinium bromide or

other cosmetically acceptable salts thereof,

~~(y) 1-(2-ethoxy-2-oxoethyl)-3-((phenylmethyl)sulfonylhydrazino carbonyl)pyridinium bromide~~

~~or other cosmetically acceptable salts thereof and~~

~~(z) 1-(2-phenyl-2-oxoethyl)-3-((phenylmethyl)sulfonylhydrazino carbonyl)pyridinium bromide~~

~~or other cosmetically acceptable salts thereof.~~

38. (amended) The method as claimed in claim 24, wherein said compound is selected from the group consisting of the following compounds:

(aa) N, N' - bis [3-carbonyl-1-(2-furan-2'-yl-2-oxoethyl)pyridinium] hydrazine dibromide or

other cosmetically acceptable salts thereof,

(ab) N, N'-bis [3-carbonyl-1-(2-thien-2'-yl-2-oxoethyl)pyridinium] hydrazine dichloride or

other cosmetically acceptable salts thereof,

(ac) N,N'-bis-[3-carbonyl-1-(2-cyclopropylamino-2-oxoethyl)pyridinium] hydrazine dichloride

or other cosmetically acceptable salts thereof,

~~(ad) 1-(2',4'-dichlorophenyl-2-oxoethyl)-3-(2-methoxyethylaminocarbonyl)pyridinium bromide~~

~~or other cosmetically acceptable salts thereof,~~

~~(ae) 1-(2-thien-2'-yl-2-oxoethyl)-3-((2-methoxyethyl)amino carbonyl)-5-bromo pyridinium~~

~~chloride or other cosmetically acceptable salts thereof,~~

(af) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,

(ag) 1-(2-thien-2'-yl-2-oxoethyl)-3-(2-(2-chloro-3-pyridoylhydrazinocarbonyl) -pyridinium chloride or other cosmetically acceptable salts thereof, and

~~(ah) 1-(2-cyclopropylamino-2-oxoethyl)-3-(2-methoxyethylaminocarbonyl)
pyridinium chloride or other cosmetically acceptable salts thereof,~~

~~(ai) 1-(2-isopropylamino-2-oxoethyl)-3-(2-methylsulfonylhydrazinocarbonyl) pyridinium
chloride or other cosmetically acceptable salts thereof,~~

~~(aj) 1-(2-phenylamino-2-oxoethyl)-3-((2-(1-oxo-3-cyclohexyl) ethyl) hydrazinocarbonyl)-
pyridinium bromide or other cosmetically acceptable salts thereof,~~

~~(ak) 1-(2-thien-2'-yl-2-oxoethyl)-3-[2-(benzoyloxy)ethylamino carbonyl] pyridinium bromide or
other cosmetically acceptable salts thereof,~~

~~(al) 1-(4-ethoxy-2,4-dioxobutyl)-3-(2-(benzoyloxy)ethylamino carbonyl) pyridinium chloride
or other cosmetically acceptable salts thereof and~~

(am) 1-(2-thien-2'-yl-2-oxoethyl)-3-[1-oxo-1-(2-methoxy carbonyl) pyridyl] hydrazino
pyridinium chloride or other cosmetically acceptable salts thereof.

39. (amended) The method as claimed in claim 24, wherein said compound is selected from the group consisting of the following compounds:

(an) 1-[1-(2-thien-2'-yl-2-oxoethyl)-5-aminocarbonyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other cosmetically acceptable

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

salts thereof,

(ao) 1-(2-thien-2'-yl-2-oxoethyl)-3-(trifluoromethanesulfonyl hydrazino carbonyl) - pyridinium bromide or other cosmetically acceptable salts thereof,

(ap) 1-[1-(2-thien-2'-yl-2-oxoethyl)-6-methyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(aq) N,N'-bis[3-carbonyl-1-(2-(5-methyl-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(ar) N,N'-bis[3-carbonyl-1-(2-(5-chloro-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(as) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-6-methyl pyridinium bromide or other cosmetically acceptable salts thereof,

(at) N,N'-bis[3-carbonyl-1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

~~(au) 1-(2-phenylamino-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,~~

(av) 1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(aw) 1-(2-(5-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,

(ax) 1-(2-(5-chloro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

bromide or other cosmetically acceptable salts thereof,

(ay) 1-(2-thien-2'-yl-2-oxoethyl)-3-(ethoxycarbonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(az) 1-(2-thien-2'-yl-2-oxoethyl)-3-(isopropylsulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(ba) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-5-bromo pyridinium bromide or other cosmetically acceptable salts thereof,

~~(bb) 1-(2-(2-ethoxy carbonyl pyrrolidin-1-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,~~

(bc) 1-(2-(5-methyl-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,

~~(bd) 1-(2-(4-carboethoxy-thiazolidin-3-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,~~

~~(be) 1-(2-(4-benzyl piperidin-1-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,~~

(bf) N,N'-(bis[3-carbonyl-1-(2-(2-ethoxycarbonyl pyrrolidin-1-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

~~(bg) 1-(2-phenylamino-2-oxoethyl)-4-[2-(benzoyloxy)-ethylamino carbonyl] pyridinium chloride or other cosmetically acceptable salts thereof,~~

(bh) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

(bi) 1-(2-thien-2(-yl-2-oxoethyl)-3-(p-methoxy phenyl sulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof;

~~(bj) 1-(2-ethoxy 2-oxoethyl)-3-(phenyl aminocarbonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof;~~

~~(bk) 1-(2-ethoxy 2-oxoethyl)-3-(p-toluene sulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof;~~

~~(bl) 1-(2-phenyl 2-oxoethyl)-3-(phenylamino carbonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof;~~

~~(bm) 1-(2-phenylamino 2-oxoethyl)-3-(benzyl sulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof;~~

~~(bn) 1-(2-phenyl 2-oxoethyl)-4-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof;~~

~~(bo) 1-(2-phenyl 2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof;~~

~~(bp) 1-(2-ethoxy 2-oxoethyl)-4-[2-(benzoyloxy) ethyl amino carbonyl] pyridinium bromide or other cosmetically acceptable salts thereof;~~

~~(bq) 1-(2-ethoxy 2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof;~~

~~(br) 1-(2-phenyl 2-oxoethyl)-3-(p-methoxyphenyl sulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof;~~

~~(bs) 1-(2-phenyl 2-oxoethyl)-4-[2-(benzoyloxy) ethyl amino carbonyl] pyridinium bromide or~~

~~other cosmetically acceptable salts thereof and~~

~~(bt) 1-(2-ethoxy-2-oxoethyl)-4-(p-methanesulfonyl-hydrazino-carbonyl)-pyridinium-bromide
or other cosmetically acceptable salts thereof~~

41. (amended) The method as claimed in claim 25, wherein said compound is selected from the group consisting of the following compounds:

(a) N,N'-bis[3-carbonyl-1-(2-thien-2'-yl-2-oxoethyl)-3-pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof,

(b) 1-(2-ethoxy-2-oxoethyl)-3-(2-(2-pyridyl)hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

~~(c) 1-(2-ethoxy-2-oxoethyl)-3-(2-(benzoyloxy)-ethylamino-carbonyl)-pyridinium-bromide or
other cosmetically acceptable salts thereof,~~

(d) N,N'-bis[3-carbonyl-1-(2-phenyl-2-oxoethyl)pyridinium]hydrazine dibromide or other cosmetically acceptable salts thereof,

~~(e) 1-(2-phenyl-2-oxoethyl)-3-(hydrazinocarbonyl)pyridinium-bromide or other cosmetically
acceptable salts thereof,~~

(f) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof, and

(g) N,N'-bis[3-carbonyl-1-(2-(2',4'-dichlorophenyl)-2-oxoethyl) pyridinium] hydrazine dibromide or other cosmetically acceptable salts thereof, .

~~(h) 1-(2-phenyl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl)-pyridinium-bromide or
other cosmetically acceptable salts thereof,~~

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

- (i) ~~1-(2-ethoxy-2-oxoethyl)-3-(methanesulfonylhydrazinocarbonyl)pyridinium bromide or other cosmetically acceptable salts thereof,~~
- (j) ~~1-(2-phenyl-2-oxoethyl)-3-(phenylsulfonylhydrazino-carbonyl)pyridinium bromide or other cosmetically acceptable salts thereof,~~
- (k) ~~1-(2-phenyl-2-oxoethyl)-2-chloro-3-(phenylsulfonylhydrazino-carbonyl)pyridinium bromide or other cosmetically acceptable salts thereof,~~
- (l) ~~1-(2-thien-2'-yl-2-oxoethyl)-4-(2-(benzoyloxy)ethylaminocarbonyl)pyridinium bromide or other cosmetically acceptable salts thereof,~~
- (m) ~~1-(2-(2,4'-dichlorophenyl)-2-oxoethyl)-3-(2-(benzoyloxy)ethylaminocarbonyl)pyridinium bromide or other cosmetically acceptable salts thereof,~~
- (n) ~~1-(2-phenyl-2-oxoethyl)-3-(2-(acetoxy)ethyloxy-carbonyl)pyridinium bromide or other cosmetically acceptable salts thereof and~~
- (o) ~~1-(2-ethoxy-2-oxoethyl)-3-(2-(benzoyloxy)ethyloxy-carbonyl)pyridinium bromide or other cosmetically acceptable salts thereof~~

42. (amended) The method as claimed in claim 25, wherein said compound is selected from the group of the following compounds:

- (p) ~~1-(2-phenylamino-2-oxoethyl)-4-(phenylsulfonylhydrazino-carbonyl)pyridinium chloride or other cosmetically acceptable salts thereof,~~
- (q) ~~1-(2-(2,4(-dichlorophenyl)-2-oxoethyl)-3-(2(methoxy)ethyloxy-carbonyl)pyridinium bromide or other cosmetically acceptable salts thereof,~~
- (r) ~~1-(2-phenylamino-2-oxoethyl)-3-((benzoyloxy)ethylaminocarbonyl)pyridinium chloride or~~

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

~~other cosmetically acceptable salts thereof,~~

(s) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylaminocarbonyl hydrazinocarbonyl) pyridinium
bromide or other cosmetically acceptable salts thereof, and

~~(t) 1-(2-phenyl-2-oxoethyl)-3-(2-(acetoxy)ethylaminocarbonyl) pyridinium bromide or other
cosmetically acceptable salts thereof,~~

~~(u) 1-(2-phenylamino-2-oxoethyl)-3-(phenylsulfonylhydrazino carbonyl) pyridinium chloride
or other cosmetically acceptable salts thereof,~~

~~(v) 1-(2-phenylamino-2-oxoethyl)-3-((4-methylphenyl)sulfonyl hydrazinocarbonyl) pyridinium
chloride or other cosmetically acceptable salts thereof,~~

~~(w) 1-(2-phenyl-2-oxoethyl)-3-(2-(benzyloxy)ethyloxy carbonyl) pyridinium bromide or other
cosmetically acceptable salts thereof,~~

(x) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylcarbonyl hydrazino carbonyl) pyridinium bromide or
other cosmetically acceptable salts thereof,

~~(y) 1-(2-ethoxy-2-oxoethyl)-3-((phenylmethyl)sulfonyl hydrazino carbonyl) pyridinium bromide
or other cosmetically acceptable salts thereof and~~

~~(z) 1-(2-phenyl-2-oxoethyl)-3-((phenylmethyl)sulfonyl hydrazino carbonyl) pyridinium bromide
or other cosmetically acceptable salts thereof.~~

43. (amended) The method as claimed in claim 25, wherein said compound is selected from
the group consisting of the following compounds:

(aa) N, N' - bis [3-carbonyl-1-(2-furan-2'-yl-2-oxoethyl) pyridinium] hydrazine dibromide or
other cosmetically acceptable salts thereof,

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

(ab) N,N'-bis [3-carbonyl -1- (2-thien-2'-yl-2-oxoethyl) pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

(ac) N,N'-bis-[3-carbonyl-1-(2-cyclopropylamino-2-oxoethyl) pyridinium] hydrazine dichloride or other cosmetically acceptable salts thereof,

~~(ad) 1 (2',4' dichlorophenyl 2-oxoethyl) 3 (2-methoxyethyl aminocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,~~

~~(ae) 1 (2-thien-2'-yl 2-oxoethyl) 3 ((2-methoxy ethyl) amino carbonyl) 5-bromo pyridinium chloride or other cosmetically acceptable salts thereof,~~

(af) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,

(ag) 1-(2-thien-2'-yl-2-oxoethyl)-3-(2-(2-chloro-3-pyridoylhydrazinocarbonyl) -pyridinium chloride or other cosmetically acceptable salts thereof, and

~~(ah) 1 (2-cyclopropylamino 2-oxoethyl) 3 (2-methoxyethylaminocarbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,~~

~~(ai) 1 (2-isopropylamino 2-oxoethyl) 3 (2-methylsulfonylhydrazinocarbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,~~

~~(aj) 1 (2-phenylamino 2-oxo-ethyl) 3 ((2 (1-oxo-3-cyclohexyl) ethyl) hydrazinocarbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,~~

~~(ak) 1 (2-thien-2'-yl 2-oxoethyl) 3 [2 (benzoyloxy)ethylamino carbonyl] pyridinium bromide or other cosmetically acceptable salts thereof,~~

~~(al) 1 (4-ethoxy 2,4-dioxobutyl) 3 (2 (benzoxylloxy)ethylamino carbonyl) pyridinium chloride~~

~~or other cosmetically acceptable salts thereof and~~

(am) 1-(2-thien-2'-yl-2-oxoethyl)-3-[1-oxo-1-(2-methoxy carbonyl) pyridyl] hydrazino
pyridinium chloride or other cosmetically acceptable salts thereof.

44. (amended) The method as claimed in claim 25, wherein said compound is selected from
the group ~~consisting~~ containing of the following compounds:

(an) 1-[1-(2-thien-2'-yl-2-oxoethyl)-5-aminocarbonyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-
yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other cosmetically acceptable
salts thereof,

(ao) 1-(2-thien-2'-yl-2-oxoethyl)-3-(trifluoromethanesulfonyl hydrazino carbonyl) - pyridinium
bromide or other cosmetically acceptable salts thereof,

(ap) 1-[1-(2-thien-2'-yl-2-oxoethyl)-6-methyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-
oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other cosmetically acceptable salts
thereof,

(aq) N,N'-bis[3-carbonyl-1-(2-(5-methyl-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine
dichloride or other cosmetically acceptable salts thereof,

(ar) N,N'-bis[3-carbonyl-1-(2-(5-chloro-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine
dichloride or other cosmetically acceptable salts thereof,

(as) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-6-methyl pyridinium
bromide or other cosmetically acceptable salts thereof,

(at) N,N'-bis[3-carbonyl-1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)pyridinium] hydrazine dichloride
or other cosmetically acceptable salts thereof,

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

~~(au) 1-(2-phenylamino-2-oxoethyl)-3-(phenylhydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,~~

(av) 1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(aw) 1-(2-(5-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,

(ax) 1-(2-(5-chloro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(ay) 1-(2-thien-2'-yl-2-oxoethyl)-3-(ethoxycarbonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(az) 1-(2-thien-2'-yl-2-oxoethyl)-3-(isopropylsulfonyl hydrazino carbonyl) pyridinium bromide or other cosmetically acceptable salts thereof,

(ba) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-5-bromo pyridinium bromide or other cosmetically acceptable salts thereof,

~~(bb) 1-(2-(2-ethoxy carbonyl pyrrolidin-1-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,~~

(bc) 1-(2-(5-methyl-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,

~~(bd) 1-(2-(4-carboethoxy thiazolidin-3-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other cosmetically acceptable salts thereof,~~

(be) 1-(2-(4-benzyl piperidin-1-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

~~pyridinium chloride or other cosmetically acceptable salts thereof,~~

(bf) N,N'-(bis[3-carbonyl-1-(2-(2-ethoxycarbonyl pyrrolidin-1-yl)-2-oxoethyl) pyridinium]

hydrazine dichloride or other cosmetically acceptable salts thereof,

(bg) ~~1-(2-phenylamino-2-oxoethyl)-4-[2-(benzoyloxy)-ethylamino-carbonyl] pyridinium
chloride or other cosmetically acceptable salts thereof,~~

(bh) 1-(2-thien-2(-yl-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other
cosmetically acceptable salts thereof, and

(bi) 1-(2-thien-2(-yl-2-oxoethyl)-3-(p-methoxy phenyl sulfonyl hydrazino carbonyl) pyridinium
bromide or other cosmetically acceptable salts thereof ;

(bj) ~~1-(2-ethoxy-2-oxoethyl)-3-(phenyl aminocarbonyl-hydrazino-carbonyl) pyridinium
bromide or other cosmetically acceptable salts thereof,~~

(bk) ~~1-(2-ethoxy-2-oxoethyl)-3-(p-toluene-sulfonyl hydrazino-carbonyl) pyridinium bromide or
other cosmetically acceptable salts thereof,~~

(bl) ~~1-(2-phenyl-2-oxoethyl)-3-(phenylamino-carbonyl hydrazino-carbonyl) pyridinium bromide
or other cosmetically acceptable salts thereof,~~

(bm) ~~1-(2-phenylamino-2-oxoethyl)-3-(benzyl sulfonyl hydrazino-carbonyl) pyridinium chloride
or other cosmetically acceptable salts thereof,~~

(bn) ~~1-(2-phenyl-2-oxoethyl)-4-(methanesulfonyl hydrazino-carbonyl) pyridinium bromide or
other cosmetically acceptable salts thereof,~~

(bo) ~~1-(2-phenyl-2-oxoethyl)-3-(phenyl hydrazino-carbonyl) pyridinium bromide
or other cosmetically acceptable salts thereof,~~

~~(bp) 1-(2-ethoxy-2-oxoethyl)-4-[2-(benzyloxy)ethyl amino carbonyl]pyridinium bromide or other cosmetically acceptable salts thereof;~~

~~(bq) 1-(2-ethoxy-2-oxoethyl)-3-(phenyl hydrazino carbonyl)pyridinium bromide or other cosmetically acceptable salts thereof;~~

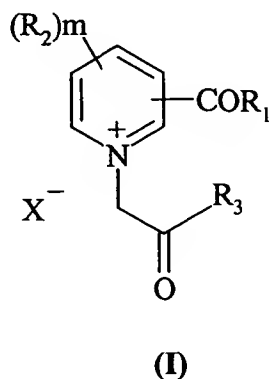
~~(br) 1-(2-phenyl-2-oxoethyl)-3-(p-methoxyphenyl sulfonyl hydrazino carbonyl)pyridinium bromide or other cosmetically acceptable salts thereof;~~

~~(bs) 1-(2-phenyl-2-oxoethyl)-4-[2-(benzyloxy)ethyl amino carbonyl]pyridinium bromide or other cosmetically acceptable salts thereof and~~

~~(bt) 1-(2-ethoxy-2-oxoethyl)-4-(p-methanesulfonyl hydrazino carbonyl)pyridinium bromide or other cosmetically acceptable salts thereof~~

49. (amended) A method of cosmetic application comprising applying an effective amount of a said composition as claimed in claim 48.

50. (amended) A pharmaceutical composition for scavenging free radicals in the body cell of a mammal comprising a compound of formula (I) or pharmaceutically acceptable salts thereof:



in admixture with pharmaceutically acceptable carrier, diluent, excipient or solvent,

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

wherein

R_1 is ~~R_4 , R_5 or $N(R_7)$~~ $N(R_7)$ R_9 and ~~Y~~ R_{11} ;

~~R_4 is selected from the group consisting of $N(R_7)R_6O$,~~

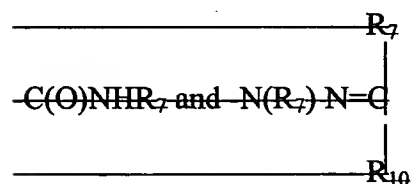
~~$N(R_7)R_6N(R_7)$,~~

~~OR_6O , and $OR_6N(R_7)$,~~

where R_6 is alkyl;

~~R_5 is selected from the group consisting of alkyl, aryl including heteroaryl, COR_7 , SO_2R_7 ,~~

~~$C(S)NHR_7$, $C(NH)NHR_7$, COR_{10} ,~~



where R_7 is selected from the group consisting of H, alkyl and aryl including heteroaryl,

provided R_7 may be the same or different for R_1 and R_3 in the same compound;

R_2 is selected from the group consisting of F, Cl, Br, I, OR_7 , NO_2 , alkyl, aryl including heteroaryl, formyl, acyl, $C(O)NR_7R_{10}$, $C(O)OR_7$, NR_7R_{10} , $N=C(R_7)(R_{10})$, SR_7 , SO_2NH_2 , SO_2 alkyl and SO_2 aryl;

m is 0, 1 or 2;

R_3 is selected from the group consisting of R_7 , OR_7 , $N(R_7)(R_{10})$, $N=C(R_7)(R_{10})$, $N(R_7)N(R_7)(R_{10})$, $N(R_7)N=C(R_7)(R_{10})$ and $CH(R_7)C(O)R_8$

where R_8 is selected from the group consisting of R_7 , OR_7 and NR_7R_{10} ;

R_9 is selected from the group consisting of hydrogen, alkyl, aryl including heteroaryl, $C(O)R_{10}$, -

SO_2R_{10} , $\text{C}(\text{S})\text{NHR}_{10}$, $\text{C}(\text{NH})\text{NH}(\text{R}_{10})$ and $\text{C}(\text{O})\text{NHR}_{10}$;

R_{10} is selected from the group consisting of H, alkyl and aryl, including heteroaryl and in each case may be the same or different from substituent R_7 , provided R_{10} may be the same or different for R_1 and R_3 in the same compound;

~~Y is selected from oxygen, NH, NR_{12} and null~~

~~R_{11} and R_{12} are independently selected from hydrogen, alkyl and aryl~~

X is selected from the group consisting of a halide ion, acetate ion, perchlorate ion, sulfonate ion, oxalate ion, citrate ion, tosylate ion, maleate ion, mesylate ion, carbonate ion, sulfite ion, phosphoric hydrogen ion, phosphonate ion, phosphate ion, ~~BF_4^-~~ BF_4^- and ~~PF_6^-~~ PF_6^- ;

with proviso that,

(i) when two alkyl groups are present on the same carbon or nitrogen, they may be linked together to form a cyclic structure;

(ii) the nitrogen of heteroaryl ring of R_{10} , when present, may be quaternized;

(iii) when R_3 is OR_7 and R_1 is $-\text{NHNH}_2$ then R_7 is not alkyl; ~~and~~

(iv) when R_3 is OR_7 , R_1 is $\text{N}(\text{R}_7)\text{N}(\text{R}_7)\text{R}_9$ and R_9 is $\text{C}(\text{O})\text{R}_{10}$ where R_{10} is alkyl, then R_7 is not hydrogen; and

(v) at least one heteroaryl group is present.

53. (amended) The composition as claimed in claim 50, wherein for ~~the~~ said compound m is 0 or 1.

54. (amended) The composition as claimed in claim 51, wherein for ~~the~~ said compound m is 0 or 1.

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

55. (amended) The composition as claimed in claim 52, wherein for ~~the~~ said compound m is 0 or 1.
56. (amended) The composition as claimed in claim 50, wherein for ~~the~~ said compound m is 0.
57. (amended) The composition as claimed in claim 51, wherein for ~~the~~ said compound m is 0.
58. (amended) The composition as claimed in claim 52, wherein for ~~the~~ said compound m is 0.
59. (amended) The composition as claimed in claim 50, wherein for ~~the~~ said compound X is a halide ion.
60. (amended) The composition as claimed in claim 50 ~~comprising compounds~~ wherein said compound is selected from the group consisting of
- (a) N,N'-bis[3-carbonyl-1-(2-thien-2'-yl-2-oxoethyl)-3-pyridinium] hydrazine dibromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
 - (b) 1-(2-ethoxy-2-oxoethyl)-3-(2-(2-pyridyl)hydrazinocarbonyl) pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
 - (c) ~~1-(2-ethoxy-2-oxoethyl)-3-(2-(benzoyloxy)-ethylamino-carbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
 - (d) N,N'-bis[3-carbonyl-1-(2-phenyl-2-oxoethyl)pyridinium]hydrazine dibromide or other pharmaceutially acceptable salts thereof,
 - (e) ~~1-(2-phenyl-2-oxoethyl)-3-(hydrazinocarbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~

(f) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof, and

(g) N,N'-bis[3-carbonyl-1-(2-(2',4'-dichlorophenyl)-2-oxoethyl) pyridinium] hydrazine dibromide or other pharmaceutially acceptable salts thereof;

~~(h) 1-(2-phenyl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof;~~

~~(i) 1-(2-ethoxy-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof;~~

~~(j) 1-(2-phenyl-2-oxoethyl)-3-(phenylsulfonylhydrazino-carbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof;~~

~~(k) 1-(2-phenyl-2-oxoethyl)-2-chloro-3-(phenylsulfonyl hydrazino-carbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof;~~

~~(l) 1-(2-thien-2'-yl-2-oxoethyl)-4-(2-(benzoyloxy) ethyl aminocarbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof;~~

~~(m) 1-(2-(2',4'-dichlorophenyl)-2-oxoethyl)-3-(2-(benzoyloxy) ethylaminocarbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof;~~

~~(n) 1-(2-phenyl-2-oxoethyl)-3-(2-(acetoxy) ethyloxy-carbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof and~~

~~(o) 1-(2-ethoxy-2-oxoethyl)-3-(2-(benzoyloxy) ethyloxy-carbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof.~~

61. (amended) The composition as claimed in claim 50 ~~comprising compounds~~ wherein said

compound is selected from the group consisting of:

- (p) ~~1-(2-phenylamino-2-oxoethyl)-4-(phenylsulfonyl hydrazino-carbonyl)pyridinium chloride or other pharmaceutially acceptable salts thereof,~~
- (q) ~~1-(2-(2,4'-dichlorophenyl)-2-oxoethyl)-3-(2(methoxy)-ethyloxy-carbonyl)-pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- (r) ~~1-(2-phenylamino-2-oxoethyl)-3-((benzoyloxy)-ethylaminocarbonyl)-pyridinium chloride or other pharmaceutially acceptable salts thereof,~~
- (s) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylaminocarbonyl hydrazinocarbonyl) pyridinium bromide or other pharmaceutially pharmaceutically acceptable salts thereof, and
- (t) ~~1-(2-phenyl-2-oxoethyl)-3-(2-(acetoxy)-ethylaminocarbonyl)-pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- (u) ~~1-(2-phenylamino-2-oxoethyl)-3-(phenyl-sulfonyl hydrazino-carbonyl)-pyridinium chloride or other pharmaceutially acceptable salts thereof,~~
- (v) ~~1-(2-phenylamino-2-oxoethyl)-3-((4-methylphenyl)sulfonyl hydrazinocarbonyl)-pyridinium chloride or other pharmaceutially acceptable salts thereof,~~
- (w) ~~1-(2-phenyl-2-oxoethyl)-3-(2-(benzoyloxy)ethyloxy-carbonyl)-pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- (x) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylcarbonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutially pharmaceutically acceptable salts thereof,
- (y) ~~1-(2-ethoxy-2-oxoethyl)-3-((phenylmethyl)sulfonyl hydrazino-carbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof and~~

~~(z) 1-(2-phenyl-2-oxoethyl)-3-((phenylmethyl)sulfonylhydrazino carbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof.~~

62. (amended) The composition as claimed in claim 50 ~~comprising compounds~~ wherein said compound is selected from the group consisting of:

(aa) N, N' - bis [3-carbonyl-1-(2-furan-2'-yl-2-oxoethyl) pyridinium] hydrazine dibromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(ab) N,N'-bis [3-carbonyl -1- (2-thien-2'-yl-2-oxoethyl) pyridinium] hydrazine dichloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(ac) N,N'-bis-[3-carbonyl-1-(2-cyclopropylamino-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutially acceptable salts thereof,

~~(ad) 1-(2',4'-dichlorophenyl-2-oxoethyl)-3-(2-methoxyethyl aminocarbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof,~~

~~(ae) 1-(2-thien-2'-yl-2-oxoethyl)-3-((2-methoxy-ethyl)-amino-carbonyl)-5-bromo-pyridinium chloride or other pharmaceutially acceptable salts thereof,~~

(af) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(ag) 1-(2-thien-2'-yl-2-oxoethyl)-3-(2-(2-chloro-3-pyridoylhydrazinocarbonyl) -pyridinium chloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof, and

~~(ah) 1-(2-cyclopropylamino-2-oxoethyl)-3-(2-methoxyethylaminocarbonyl) -pyridinium chloride or other pharmaceutially acceptable salts thereof,~~

~~(ai) 1-(2-isopropylamino-2-oxoethyl)-3-(2-methylsulfonylhydrazinocarbonyl) pyridinium~~

~~chloride or other pharmaceutially acceptable salts thereof,~~

~~(aj) 1-(2-phenylamino-2-oxo-ethyl)-3-((2-(1-oxo-3-cyclohexyl)-ethyl)-hydrazinocarbonyl)-pyridinium bromide or other pharmaceutially acceptable salts thereof,~~

~~(ak) 1-(2-thien-2'-yl-2-oxoethyl)-3-[2-(benzoyloxy)ethylamino-carbonyl]-pyridinium bromide or other pharmaceutially acceptable salts thereof,~~

~~(al) 1-(4-ethoxy-2,4-dioxobutyl)-3-(2-(benzoyloxy)ethylamino-carbonyl)-pyridinium chloride or other pharmaceutially acceptable salts thereof and~~

(am) 1-(2-thien-2'-yl-2-oxoethyl)-3-[1-oxo-1-(2-methoxy carbonyl) pyridyl] hydrazino pyridinium chloride or other pharmaceutially pharmaceutically acceptable salts thereof.

63. (amended) The composition as claimed in claim 50 comprising compounds wherein said compound is selected from the group consisting of:

(an) 1-[1-(2-thien-2'-yl-2-oxoethyl)-5-aminocarbonyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other pharmaceutially pharmaceutically acceptable salts thereof,

(ao) 1-(2-thien-2'-yl-2-oxoethyl)-3-(trifluoromethanesulfonyl hydrazino carbonyl) - pyridinium bromide or other pharmaceutially pharmaceutically acceptable salts thereof,

(ap) 1-[1-(2-thien-2'-yl-2-oxoethyl)-6-methyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other pharmaceutially pharmaceutically acceptable salts thereof,

(aq) N,N'-bis[3-carbonyl-1-(2-(5-methyl-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutially pharmaceutically acceptable salts thereof,

- (ar) N,N'-bis[3-carbonyl-1-(2-(5-chloro-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
- (as) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-6-methyl pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
- (at) N,N'-bis[3-carbonyl-1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)pyridinium] hydrazine dichloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
- ~~(au) 1-(2-phenylamino-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium chloride or other pharmaceutially acceptable salts thereof,~~
- (av) 1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
- (aw) 1-(2-(5-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
- (ax) 1-(2-(5-chloro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
- (ay) 1-(2-thien-2'-yl-2-oxoethyl)-3-(ethoxycarbonyl hydrazino carbonyl) pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
- (az) 1-(2-thien-2'-yl-2-oxoethyl)-3-(isopropylsulfonyl hydrazino carbonyl) pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
- (ba) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-5-bromo pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
- ~~(bb) 1-(2-(2-ethoxy carbonyl pyrrolidin-1-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino~~

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

~~carbonyl) pyridinium chloride or other pharmaceutially acceptable salts thereof,~~

(bc) 1-(2-(5-methyl-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

~~(bd) 1-(2-(4-carboethoxy-thiazolidin-3-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutially acceptable salts thereof,~~

~~(be) 1-(2-(4-benzyl-piperidin-1-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,~~

(bf) N,N'-(bis[3-carbonyl-1-(2-(2-ethoxycarbonyl pyrrolidin-1-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

~~(bg) 1-(2-phenylamino-2-oxoethyl)-4-[2-(benzoyloxy)-ethylamino-carbonyl] pyridinium chloride or other pharmaceutically acceptable salts thereof,~~

(bh) 1-(2-thien-2(-yl-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof, and

(bi) 1-(2-thien-2(-yl-2-oxoethyl)-3-(p-methoxy phenyl sulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

~~(bj) 1-(2-ethoxy-2-oxoethyl)-3-(phenyl aminocarbonyl-hydrazino-carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(bk) 1-(2-ethoxy-2-oxoethyl)-3-(p-toluene-sulfonyl hydrazino-carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(bl) 1-(2-phenyl-2-oxoethyl)-3-(phenylamino-carbonyl-hydrazino-carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(bm) 1-(2-phenylamino-2-oxoethyl)-3-(benzyl-sulfonyl hydrazino-carbonyl)~~

~~pyridiniumchloride or other pharmaceutically acceptable salts thereof;~~

~~(bn) 1-(2-phenyl-2-oxoethyl)-4-(methanesulfonyl hydrazino-carbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(bo) 1-(2-phenyl-2-oxoethyl)-3-(phenyl hydrazino-carbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(bp) 1-(2-ethoxy-2-oxoethyl)-4-[2-(benzoyloxy)-ethyl-amino-carbonyl]-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

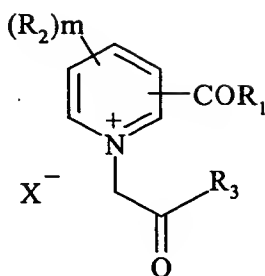
~~(bq) 1-(2-ethoxy-2-oxoethyl)-3-(phenyl hydrazino-carbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(br) 1-(2-phenyl-2-oxoethyl)-3-(p-methoxyphenyl-sulfonyl hydrazino-carbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(bs) 1-(2-phenyl-2-oxoethyl)-4-[2-(benzoyloxy)-ethyl-amino-carbonyl]-pyridinium bromide or other pharmaceutically acceptable salts thereof and~~

~~(bt) 1-(2-ethoxy-2-oxoethyl)-4-(p-methanesulfonyl hydrazino-carbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof.~~

65. (amended) A method of scavenging free radical in the body cells comprising administering to a mammal in need of scavenging free radical from its body cells an effective amount of a compound of formula (I)



(I)

or pharmaceutically acceptable salts thereof and a pharmaceutically acceptable carrier, diluent, excipient or solvent,

wherein

~~R₁ is -R₄-R₅ or -N(R₇) N (R₇) R₉ and Y-R₁₁;~~

~~R₄ is selected from the group consisting of -N(R₇)R₆O-,~~

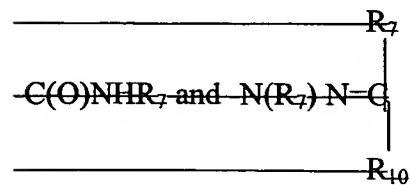
~~-N(R₇)R₆N(R₇),~~

~~-OR₆O-, and -OR₆N(R₇)-,~~

where R₆ is alkyl;

~~R₅ is selected from the group consisting of alkyl, aryl including heteroaryl, -COR₇, -SO₂R₇,~~

~~C(S)NHR₇, -C(NH)NHR₇, -COR₁₀,~~



where R₇ is selected from the group consisting of H, alkyl and aryl including heteroaryl,

provided R_7 may be the same or different for R_1 and R_3 in the same compound;

R_2 is selected from the group consisting of F, Cl, Br, I, OR_7 , NO_2 , alkyl, aryl including heteroaryl, formyl, acyl, $C(O)NR_7R_{10}$, $C(O)OR_7$, NR_7R_{10} , $N=C(R_7)(R_{10})$, SR_7 , SO_2NH_2 , SO_2 alkyl and SO_2 aryl;

m is 0, 1 or 2;

R_3 is selected from the group consisting of R_7 , OR_7 , $N(R_7)(R_{10})$, $N=C(R_7)(R_{10})$, $N(R_7)N(R_7)(R_{10})$, $N(R_7)N=C(R_7)(R_{10})$ and $CH(R_7)C(O)R_8$

where R_8 is selected from the group consisting of R_7 , OR_7 and NR_7R_{10} ;

R_9 is selected from the group consisting of hydrogen, alkyl, aryl including heteroaryl, $C(O)R_{10}$, SO_2R_{10} , $C(S)NHR_{10}$, $C(NH)NH(R_{10})$ and $C(O)NHR_{10}$;

R_{10} is selected from the group consisting of H, alkyl and aryl, including heteroaryl and in each case may be the same or different from substituent R_7 , provided R_{10} may be the same or different for R_1 and R_3 in the same compound;

~~Y is selected from oxygen, NH, NR_{12} and null~~

~~R_{11} and R_{12} are independently selected from hydrogen, alkyl and aryl~~

X is selected from the group consisting of a halide ion, acetate ion, perchlorate ion, sulfonate ion, oxalate ion, citrate ion, tosylate ion, maleate ion, mesylate ion, carbonate ion, sulfite ion, phosphoric hydrogen ion, phosphonate ion, phosphate ion, BF_4^- BF_4^- and PF_6^- PF_6^- ;

with proviso that,

(i) when two alkyl groups are present on the same carbon or nitrogen, they may be linked together to form a cyclic structure;

- (ii) the nitrogen of heteroaryl ring of R₁₀, when present, may be quaternized;
- (iii) when R₃ is OR₇ and R₁ is -NHNH₂ then R₇ is not alkyl; ~~and~~
- (iv) when R₃ is OR₇, R₁ is N(R₇)N(R₇)R₉ and R₉ is C(O)R₁₀ where R₁₀ is alkyl, then R₇ is not hydrogen; and
- (v) at least one heteroaryl group is present.

66. (amended) The method as claimed in claim 65, ~~comprising compounds wherein said~~
compound is selected from the group consisting of;

- (a) N,N'-bis[3-carbonyl-1-(2-thien-2'-yl-2-oxoethyl)-3-pyridinium] hydrazine dibromide or other pharmaceutically acceptable salts thereof,
- (b) 1-(2-ethoxy-2-oxoethyl)-3-(2-(2-pyridyl)hydrazinocarbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,
- ~~(c) 1-(2-ethoxy-2-oxoethyl)-3-(2-(benzoyloxy)ethylamino-carbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof,~~
- (d) N,N'-bis[3-carbonyl-1-(2-phenyl-2-oxoethyl)pyridinium]hydrazine dibromide or other pharmaceutically acceptable salts thereof,
- ~~(e) 1-(2-phenyl-2-oxoethyl)-3-(hydrazinocarbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof,~~
- (f) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof, and
- (g) N,N'-bis[3-carbonyl-1-(2-(2',4'-dichlorophenyl)-2-oxoethyl) pyridinium] hydrazine dibromide or other pharmaceutically acceptable salts thereof,

~~(h) 1-(2-phenyl-2-oxoethyl)-3-(methanesulfonylhydrazinocarbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(i) 1-(2-ethoxy-2-oxoethyl)-3-(methanesulfonylhydrazinocarbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(j) 1-(2-phenyl-2-oxoethyl)-3-(phenylsulfonylhydrazino-carbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(k) 1-(2-phenyl-2-oxoethyl)-2-chloro-3-(phenylsulfonylhydrazino-carbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(l) 1-(2-thien-2'-yl-2-oxoethyl)-4-(2-(benzoyloxy)-ethylaminocarbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(m) 1-(2-(2,4'-dichlorophenyl)-2-oxoethyl)-3-(2-(benzoyloxy)-ethylaminocarbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(n) 1-(2-phenyl-2-oxoethyl)-3-(2-(acetoxy)-ethyloxy-carbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof and~~

~~(o) 1-(2-ethoxy-2-oxoethyl)-3-(2-(benzoyloxy)-ethyloxy carbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof.~~

67. (amended) The method as claimed in claim 65, comprising compounds wherein said compound is selected from the group consisting of:

~~(p) 1-(2-phenylamino-2-oxoethyl)-4-(phenylsulfonylhydrazino-carbonyl)pyridinium chloride or other pharmaceutically acceptable salts thereof;~~

~~(q) 1-(2-(2,4'-dichlorophenyl)-2-oxoethyl)-3-(2(methoxy)-ethyloxycarbonyl)pyridinium~~

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appln. No. 09/995,731

~~bromide or other pharmaceutically acceptable salts thereof,~~

~~(r) 1-(2-phenylamino-2-oxoethyl)-3-((benzoyloxy)ethylaminocarbonyl)pyridinium chloride or other pharmaceutically acceptable salts thereof,~~

~~(s) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylaminocarbonyl hydrazinocarbonyl) pyridinium~~

~~bromide or other pharmaceutically acceptable salts thereof, and~~

~~(t) 1-(2-phenyl-2-oxoethyl)-3-(2-(acetoxy)ethylaminocarbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(u) 1-(2-phenylamino-2-oxoethyl)-3-(phenylsulfonylhydrazino-carbonyl)pyridinium chloride or other pharmaceutically acceptable salts thereof,~~

~~(v) 1-(2-phenylamino-2-oxoethyl)-3-((4-methylphenyl)sulfonylhydrazinocarbonyl)pyridinium chloride or other pharmaceutically acceptable salts thereof,~~

~~(w) 1-(2-phenyl-2-oxoethyl)-3-(2-(benzoyloxy)ethyloxy-carbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(x) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylcarbonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(y) 1-(2-ethoxy-2-oxoethyl)-3-((phenylmethyl)sulfonylhydrazino-carbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof and~~

~~(z) 1-(2-phenyl-2-oxoethyl)-3-((phenylmethyl)sulfonylhydrazino-carbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof.~~

68. (amended) The method as claimed in claim 65, ~~comprising compounds~~ wherein said compound is selected from the group consisting of:

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appln. No. 09/995,731

(aa) N, N' - bis [3-carbonyl-1-(2-furan-2'-yl-2-oxoethyl) pyridinium] hydrazine dibromide or other pharmaceutically acceptable salts thereof,

(ab) N,N'-bis [3-carbonyl -1- (2-thien-2'-yl-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(ac) N,N'-bis-[3-carbonyl-1-(2-cyclopropylamino-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

~~(ad) 1-(2',4'-dichlorophenyl-2-oxoethyl)-3-(2-methoxyethyl-aminocarbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(ae) 1-(2-thien-2'-yl-2-oxoethyl)-3-((2-methoxy-ethyl)-amino-carbonyl)-5-bromo-pyridinium chloride or other pharmaceutically acceptable salts thereof,~~

(af) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,

(ag) 1-(2-thien-2'-yl-2-oxoethyl)-3-(2-(2-chloro-3-pyridoylhydrazinocarbonyl) -pyridinium chloride or other pharmaceutically acceptable salts thereof, and

~~(ah) 1-(2-cyclopropylamino-2-oxoethyl)-3-(2-methoxyethylaminocarbonyl)-pyridinium chloride or other pharmaceutically acceptable salts thereof,~~

~~(ai) 1-(2-isopropylamino-2-oxoethyl)-3-(2-methylsulfonylhydrazinocarbonyl)-pyridinium chloride or other pharmaceutically acceptable salts thereof,~~

~~(aj) 1-(2-phenylamino-2-oxo-ethyl)-3-((2-(1-oxo-3-cyclohexyl)-ethyl)-hydrazinocarbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(ak) 1-(2-thien-2'-yl-2-oxoethyl)-3-[2-(benzoyloxy)ethylamino-carbonyl]-pyridinium bromide or~~

~~other pharmaceutically acceptable salts thereof,~~

~~(al) 1-(4-ethoxy-2,4-dioxobutyl)-3-(2-(benzoxyleoxy)ethylamino-carbonyl)-pyridinium chloride~~

~~or other pharmaceutically acceptable salts thereof and~~

(am) 1-(2-thien-2'-yl-2-oxoethyl)-3-[1-oxo-1-(2-methoxy carbonyl) pyridyl] hydrazino
pyridinium chloride or other pharmaceutically acceptable salts thereof.

69. (amended) The method as claimed in claim 65 ~~comprising compounds~~ wherein said compound is selected from the group consisting of:

(an) 1-[1-(2-thien-2'-yl-2-oxoethyl)-5-aminocarbonyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(ao) 1-(2-thien-2'-yl-2-oxoethyl)-3-(trifluoromethanesulfonyl hydrazino carbonyl) - pyridinium bromide or other pharmaceutically acceptable salts thereof,

(ap) 1-[1-(2-thien-2'-yl-2-oxoethyl)-6-methyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(aq) N,N'-bis[3-carbonyl-1-(2-(5-methyl-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(ar) N,N'-bis[3-carbonyl-1-(2-(5-chloro-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(as) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-6-methyl pyridinium bromide or other pharmaceutically acceptable salts thereof,

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

(at) N,N'-bis[3-carbonyl-1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

~~(au) 1-(2-phenylamino-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,~~

(av) 1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(aw) 1-(2-(5-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,

(ax) 1-(2-(5-chloro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(ay) 1-(2-thien-2'-yl-2-oxoethyl)-3-(ethoxycarbonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(az) 1-(2-thien-2'-yl-2-oxoethyl)-3-(isopropylsulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(ba) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-5-bromo pyridinium bromide or other pharmaceutically acceptable salts thereof,

~~(bb) 1-(2-(2-ethoxy carbonyl pyrrolidin-1-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,~~

(bc) 1-(2-(5-methyl-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,

(bd) 1-(2-(4 [carbethoxy] ~~carboethoxy~~ thiazolidin-3-yl)-2-oxoethyl)-3-(methanesulfonyl

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

~~hydrazino-carbonyl)-pyridinium-chloride or other pharmaceutically acceptable salts thereof,~~

~~(be) 1-(2-(4-benzyl-piperidin-1-yl)-2-oxoethyl)-3-(methanesulfonyl-hydrazino-carbonyl)~~

~~pyridinium-chloride or other pharmaceutically acceptable salts thereof,~~

~~(bf) N,N'-bis[3-carbonyl-1-(2-(2-ethoxycarbonyl-pyrrolidin-1-yl)-2-oxoethyl)-pyridinium]~~

~~hydrazine dichloride or other pharmaceutically acceptable salts thereof,~~

~~(bg) 1-(2-phenylamino-2-oxoethyl)-4-[2-(benzoyloxy)-ethylamino-carbonyl]-pyridinium~~

~~chloride or other pharmaceutically acceptable salts thereof,~~

~~(bh) 1-(2-thien-2(-yl)-2-oxoethyl)-3-(phenyl-hydrazino-carbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof, and~~

~~(bi) 1-(2-thien-2(-yl)-2-oxoethyl)-3-(p-methoxy-phenyl-sulfonyl-hydrazino-carbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(bj) 1-(2-ethoxy-2-oxoethyl)-3-(phenyl-aminocarbonyl-hydrazino-carbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(bk) 1-(2-ethoxy-2-oxoethyl)-3-(p-toluene-sulfonyl-hydrazino-carbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(bl) 1-(2-phenyl-2-oxoethyl)-3-(phenylamino-carbonyl-hydrazino-carbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(bm) 1-(2-phenylamino-2-oxoethyl)-3-(benzyl-sulfonyl-hydrazino-carbonyl)-pyridinium-chloride or other pharmaceutically acceptable salts thereof,~~

~~(bn) 1-(2-phenyl-2-oxoethyl)-4-(methanesulfonyl-hydrazino-carbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(be) 1-(2-phenyl-2-oxoethyl)-3-(phenylhydrazino-carbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(bp) 1-(2-ethoxy-2-oxoethyl)-4-[2-(benzyloxy)-ethyl-amino-carbonyl]-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

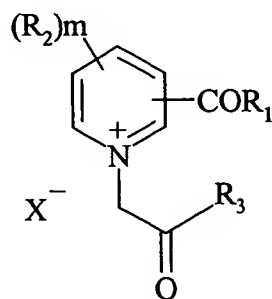
~~(bq) 1-(2-ethoxy-2-oxoethyl)-3-(phenylhydrazino-carbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(br) 1-(2-phenyl-2-oxoethyl)-3-(p-methoxyphenyl-sulfonyl-hydrazino-carbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(bs) 1-(2-phenyl-2-oxoethyl)-4-[2-(benzyloxy)-ethyl-amino-carbonyl]-pyridinium bromide or other pharmaceutically acceptable salts thereof and~~

~~(bt) 1-(2-ethoxy-2-oxoethyl)-4-(p-methanesulfonyl-hydrazino-carbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof.~~

71. (amended) A method of treating diseases caused by accumulation of free radicals in the body cells of a mammal comprising treating a mammal affected by such disease with an effective amount of a compound of formula (I)



(I)

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

or its pharmaceutically acceptable salts and a pharmaceutically acceptable carrier, diluent, excipient or solvent,

wherein

R_1 is ~~R_4 , R_5 or $N(R_7)N(R_7)R_9$ and $Y-R_{11}$;~~

~~R_4 is selected from the group consisting of $N(R_7)R_6O$,~~

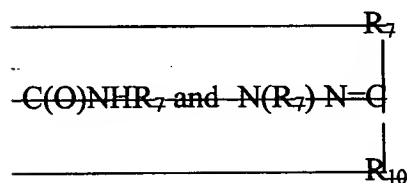
~~$N(R_7)R_6N(R_7)$,~~

~~OR_6O , and $OR_6N(R_7)$,~~

where R_6 is alkyl;

~~R_5 is selected from the group consisting of alkyl, aryl including heteroaryl, COR_7 , SO_2R_7 ,~~

~~$C(S)NHR_7$, $C(NH)NHR_7$, COR_{10} ;~~



where R_7 is selected from the group consisting of H, alkyl and aryl including heteroaryl, provided R_7 may be the same or different for R_1 and R_3 in the same compound;

R_2 is selected from the group consisting of F, Cl, Br, I, OR_7 , NO_2 , alkyl, aryl including heteroaryl, formyl, acyl, $C(O)NR_7R_{10}$, $C(O)OR_7$, NR_7R_{10} , $N=C(R_7)(R_{10})$, SR_7 , SO_2NH_2 , SO_2 alkyl and SO_2 aryl;

m is 0, 1 or 2;

R_3 is selected from the group consisting of R_7 , OR_7 , $N(R_7)(R_{10})$, $N=C(R_7)(R_{10})$,

$N(R_7)N(R_7)(R_{10})$, $N(R_7)N=C(R_7)(R_{10})$ and $CH(R_7)C(O)R_8$

where R_8 is selected from the group consisting of R_7 , OR_7 and NR_7R_{10} ;

R_9 is selected from the group consisting of hydrogen, alkyl, aryl including heteroaryl, $C(O)R_{10}$, -
 SO_2R_{10} , $C(S)NHR_{10}$, $C(NH)NH(R_{10})$ and $C(O)NHR_{10}$;

R_{10} is selected from the group consisting of H, alkyl and aryl, including heteroaryl and in each case may be the same or different from substituent R_7 , provided R_{10} may be the same or different for R_1 and R_3 in the same compound;

~~Y is selected from oxygen, NH, NR_{12} and null~~

~~R_{11} and R_{12} are independently selected from hydrogen, alkyl and aryl~~

X is selected from the group consisting of a halide ion, acetate ion, perchlorate ion, sulfonate ion, oxalate ion, citrate ion, tosylate ion, maleate ion, mesylate ion, carbonate ion, sulfite ion, phosphoric hydrogen ion, phosphonate ion, phosphate ion, BF_4^- and PF_6^- ;

with proviso that,

(i) when two alkyl groups are present on the same carbon or nitrogen, they may be linked together to form a cyclic structure;

(ii) the nitrogen of heteroaryl ring of R_{10} , when present, may be quaternized;

(iii) when R_3 is OR_7 and R_1 is $-NHNH_2$ then R_7 is not alkyl; ~~and~~

(iv) when R_3 is OR_7 , R_1 is $N(R_7)N(R_7)R_9$ and R_9 is $C(O)R_{10}$ where R_{10} is alkyl, then R_7 is not hydrogen; and

(v) at least one heteroaryl group is present.

72. (amended) The method as claimed in claim 71 ~~comprising compounds~~ wherein said compound is selected from the group consisting of:

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

- (a) N,N'-bis[3-carbonyl-1-(2-thien-2'-yl-2-oxoethyl)-3-pyridinium] hydrazine dibromide or other pharmaceutically acceptable salts thereof,
- (b) 1-(2-ethoxy-2-oxoethyl)-3-(2-(2-pyridyl)hydrazinocarbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,
- ~~(c) 1-(2-ethoxy-2-oxoethyl)-3-(2-(benzoyloxy)ethylamino-carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,~~
- (d) N,N'-bis[3-carbonyl-1-(2-phenyl-2-oxoethyl)pyridinium]hydrazine dibromide or other pharmaceutically acceptable salts thereof,
- ~~(e) 1-(2-phenyl-2-oxoethyl)-3-(hydrazinocarbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof,~~
- (f) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof, and
- (g) N,N'-bis[3-carbonyl-1-(2-(2',4'-dichlorophenyl)-2-oxoethyl) pyridinium] hydrazine dibromide or other pharmaceutically acceptable salts thereof,
- ~~(h) 1-(2-phenyl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,~~
- ~~(i) 1-(2-ethoxy-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,~~
- ~~(j) 1-(2-phenyl-2-oxoethyl)-3-(phenylsulfonylhydrazino-carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,~~
- (k) 1-(2-phenyl-2-oxoethyl)-2-chloro-3-(phenylsulfonyl hydrazino-carbonyl) pyridinium bromide

~~or other pharmaceutically acceptable salts thereof,~~

~~(l) 1-(2-thien-2'-yl-2-oxoethyl)-4-(2-(benzoyloxy)ethyl aminocarbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(m) 1-(2-(2,4'-dichlorophenyl)-2-oxoethyl)-3-(2-(benzoyloxy)ethylaminocarbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(n) 1-(2-phenyl-2-oxoethyl)-3-(2-(acetoxy)ethyloxy)carbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof and~~

~~(o) 1-(2-ethoxy-2-oxoethyl)-3-(2-(benzoyloxy)ethyloxy carbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof.~~

73. (amended) The method as claimed in claim 71 ~~comprising compounds~~ wherein said compound is selected from the group consisting of:

~~(p) 1-(2-phenylamino-2-oxoethyl)-4-(phenylsulfonyl hydrazino carbonyl)pyridinium chloride or other pharmaceutically acceptable salts thereof,~~

~~(q) 1-(2-(2,4'-dichlorophenyl)-2-oxoethyl)-3-(2(methoxy)ethyloxy carbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(r) 1-(2-phenylamino-2-oxoethyl)-3-((benzoyloxy)ethylaminocarbonyl)pyridinium chloride or other pharmaceutically acceptable salts thereof,~~

~~(s) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylaminocarbonyl hydrazinocarbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof, and~~

~~(t) 1-(2-phenyl-2-oxoethyl)-3-(2-(acetoxy)ethylaminocarbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(u) 1-(2-phenylamino-2-oxoethyl)-3-(phenylsulfonylhydrazinocarbonyl)pyridinium chloride or other pharmaceutically acceptable salts thereof;~~

~~(v) 1-(2-phenylamino-2-oxoethyl)-3-((4-methylphenyl)sulfonylhydrazinocarbonyl)pyridinium chloride or other pharmaceutically acceptable salts thereof;~~

~~(w) 1-(2-phenyl-2-oxoethyl)-3-(2-(benzoyloxy)ethyloxy carbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

(x) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylcarbonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof;

~~(y) 1-(2-ethoxy-2-oxoethyl)-3-((phenylmethyl)sulfonylhydrazino carbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof and~~

(z) 1-(2-phenyl-2-oxoethyl)-3-((phenylmethyl)sulfonyl hydrazino carbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof.

74. (amended) The method as claimed in claim 71 comprising compounds wherein said compound is selected from the group consisting of:

(aa) N, N' - bis [3-carbonyl-1-(2-furan-2'-yl-2-oxoethyl) pyridinium] hydrazine dibromide or other pharmaceutically acceptable salts thereof,

(ab) N,N'-bis [3-carbonyl -1- (2-thien-2'-yl-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(ac) N,N'-bis-[3-carbonyl-1-(2-cyclopropylamino-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

~~(ad) 1-(2',4'-dichlorophenyl-2-oxoethyl)-3-(2-methoxyethyl aminocarbonyl)-pyridinium bromide~~

~~or other pharmaceutically acceptable salts thereof,~~

~~(ae) 1-(2-thien-2'-yl-2-oxoethyl)-3-((2-methoxy-ethyl)-amino-carbonyl)-5-bromo-pyridinium
chloride or other pharmaceutically acceptable salts thereof,~~

(af) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or
other pharmaceutically acceptable salts thereof,

(ag) 1-(2-thien-2'-yl-2-oxoethyl)-3-(2-(2-chloro-3-pyridoyl)hydrazinocarbonyl) -pyridinium
chloride or other pharmaceutically acceptable salts thereof,

(ah) 1-(2-cyclopropylamino-2-oxoethyl)-3-(2-methoxyethylaminocarbonyl)-pyridinium chloride
or other pharmaceutically acceptable salts thereof, and

~~(ai) 1-(2-isopropylamino-2-oxoethyl)-3-(2-methylsulfonylhydrazinocarbonyl)-pyridinium
chloride or other pharmaceutically acceptable salts thereof,~~

~~(aj) 1-(2-phenylamino-2-oxo-ethyl)-3-({2-(1-oxo-3-cyclohexyl)-ethyl}-hydrazinocarbonyl)-
pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(ak) 1-(2-thien-2'-yl-2-oxoethyl)-3-[2-(benzoyloxy)ethylamino-carbonyl]-
pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(al) 1-(4-ethoxy-2,4-dioxobutyl)-3-(2-(benzoyloxy)ethylamino-carbonyl)-pyridinium chloride
or other pharmaceutically acceptable salts thereof and~~

(am) 1-(2-thien-2'-yl-2-oxoethyl)-3-[1-oxo-1-(2-methoxy carbonyl) pyridyl] hydrazino
pyridinium chloride or other pharmaceutically acceptable salts thereof.

75. (amended) The method as claimed in claim 71 comprising compounds wherein said
compound is selected from the group consisting of:

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

(an) 1-[1-(2-thien-2'-yl-2-oxoethyl)-5-aminocarbonyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(ao) 1-(2-thien-2'-yl-2-oxoethyl)-3-(trifluoromethanesulfonyl hydrazino carbonyl) - pyridinium bromide or other pharmaceutically acceptable salts thereof,

(ap) 1-[1-(2-thien-2'-yl-2-oxoethyl)-6-methyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(aq) N,N'-bis[3-carbonyl-1-(2-(5-methyl-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(ar) N,N'-bis[3-carbonyl-1-(2-(5-chloro-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

(as) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-6-methyl pyridinium bromide or other pharmaceutically acceptable salts thereof,

(at) N,N'-bis[3-carbonyl-1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

~~(au) 1-(2-phenylamino-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,~~

(av) 1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(aw) 1-(2-(5-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium

chloride or other pharmaceutically acceptable salts thereof,

(ax) 1-(2-(5-chloro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(ay) 1-(2-thien-2'-yl-2-oxoethyl)-3-(ethoxycarbonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(az) 1-(2-thien-2'-yl-2-oxoethyl)-3-(isopropylsulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,

(ba) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-5-bromo pyridinium bromide or other pharmaceutically acceptable salts thereof,

~~(bb) 1-(2-(2-ethoxy carbonyl pyrrolidin-1-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,~~

(bc) 1-(2-(5-methyl-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,

~~(bd) 1-(2-(4-carboethoxy-thiazolidin-3-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,~~

~~(be) 1-(2-(4-benzyl-piperidin-1-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,~~

(bf) N,N'-bis[3-carbonyl-1-(2-(2-ethoxycarbonyl pyrrolidin-1-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

~~(bg) 1-(2-phenylamino-2-oxoethyl)-4-[2-(benzoyloxy)-ethylamino carbonyl] pyridinium chloride or other pharmaceutically acceptable salts thereof,~~

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

- (bh) 1-(2-thien-2(-yl-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof, and
- (bi) 1-(2-thien-2(-yl-2-oxoethyl)-3-(p-methoxy phenyl sulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof;
- ~~(bj) 1 (2 ethoxy 2 oxoethyl) 3 (phenyl aminocarbonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof;~~
- ~~(bk) 1 (2 ethoxy 2 oxoethyl) 3 (p-toluene sulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof;~~
- ~~(bl) 1 (2-phenyl 2-oxoethyl) 3 (phenylamino carbonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof;~~
- ~~(bm) 1 (2-phenylamino 2-oxoethyl) 3 (benzyl sulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof;~~
- ~~(bn) 1 (2-phenyl 2-oxoethyl) 4 (methanesulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof;~~
- ~~(bo) 1 (2-phenyl 2-oxoethyl) 3 (phenyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof;~~
- ~~(bp) 1 (2-ethoxy 2-oxoethyl) 4 [2-(benzoyloxy) ethyl amino carbonyl] pyridinium bromide or other pharmaceutically acceptable salts thereof;~~
- ~~(bq) 1 (2-ethoxy 2-oxoethyl) 3 (phenyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof;~~
- (br) 1-(2-phenyl 2-oxoethyl) 3-(p-methoxyphenyl sulfonyl hydrazino carbonyl) pyridinium

~~bromide or other pharmaceutically acceptable salts thereof,~~

~~(bs) 1-(2-phenyl-2-oxoethyl)-4-[2-(benzyloxy)ethylamino-carbonyl]pyridinium bromide or other pharmaceutically acceptable salts thereof and~~

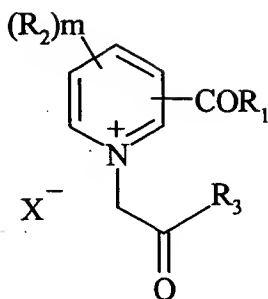
~~(bt) 1-(2-ethoxy-2-oxoethyl)-4-(p-methanesulfonyl-hydrazino-carbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof.~~

77. (amended) The pharmaceutical composition as claimed in claim 50 in the form of an oral formulation, wherein the carrier, diluent, excipient or solvent is one acceptable for oral administration.

79. (amended) The pharmaceutical composition as claimed in claim 50 in the form of a parenteral formulation, wherein the carrier, diluent, excipient or solvent is one acceptable for parenteral administration.

81. (amended) The pharmaceutical composition as claimed in claim 50 in the form of a lotion, oral rinse ~~and~~ or toothpaste, wherein the carrier, diluent, excipient or solvent is one acceptable for use in lotion, oral rinse or toothpaste.

83. (amended) A method of inhibiting the formation of AGE (Advanced Glycation End products) in a mammal which comprises administering an effective amount of a compound of Formula (I)



(I)

or its pharmaceutically acceptable salts in association with a pharmaceutically acceptable carrier, diluent, excipient or solvent,

wherein

R_1 is ~~R_4 , R_5 or $N(R_7)$~~ $N(R_7)$ R_9 and ~~Y~~ R_{11} ;

R_4 is selected from the group consisting of ~~$N(R_7)R_6O$,~~

~~$N(R_7)R_6N(R_7)$,~~

~~OR_6O , and $OR_6N(R_7)$,~~

where R_6 is alkyl;

R_5 is selected from the group consisting of alkyl, aryl including heteroaryl, ~~COR_7 , SO_2R_7 ,~~

~~$C(S)NHR_7$, $C(NH)NHR_7$, COR_{10} ,~~

~~$C(O)NHR_7$ and $N(R_7)N=C$~~
 R_7
 R_{10}

where R_7 is selected from the group consisting of H, alkyl and aryl including heteroaryl,

provided R_7 may be the same or different for R_1 and R_3 in the same compound;

R_2 is selected from the group consisting of F, Cl, Br, I, OR_7 , NO_2 , alkyl, aryl including

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

heteroaryl, formyl, acyl, $C(O)NR_7R_{10}$, $C(O)OR_7$, NR_7R_{10} , $N=C(R_7)(R_{10})$, SR_7 , SO_2NH_2 , SO_2 alkyl and SO_2 aryl;

m is 0, 1 or 2;

R_3 is selected from the group consisting of R_7 , OR_7 , $N(R_7)(R_{10})$, $N=C(R_7)(R_{10})$,

$N(R_7)N(R_7)(R_{10})$, $N(R_7)N=C(R_7)(R_{10})$ and $CH(R_7)C(O)R_8$

where R_8 is selected from the group consisting of R_7 , OR_7 and NR_7R_{10} ;

R_9 is selected from the group consisting of hydrogen, alkyl, aryl including heteroaryl, $C(O)R_{10}$, SO_2R_{10} , $C(S)NHR_{10}$, $C(NH)NH(R_{10})$ and $C(O)NHR_{10}$;

R_{10} is selected from the group consisting of H, alkyl and aryl, including heteroaryl and in each case may be the same or different from substituent R_7 , provided R_{10} may be the same or different for R_1 and R_3 in the same compound;

~~Y is selected from oxygen, NH, NR_{12} and null~~

~~R_{11} and R_{12} are independently selected from hydrogen, alkyl and aryl~~

X is selected from the group consisting of a halide ion, acetate ion, perchlorate ion, sulfonate ion, oxalate ion, citrate ion, tosylate ion, maleate ion, mesylate ion, carbonate ion, sulfite ion, phosphoric hydrogen ion, phosphonate ion, phosphate ion, BF_4^- , BF_4^- and PF_6^- , PF_6^- ;

with proviso that,

- (i) when two alkyl groups are present on the same carbon or nitrogen, they may be linked together to form a cyclic structure;
- (ii) the nitrogen of heteroaryl ring of R_{10} , when present, may be quaternized;
- (iii) when R_3 is OR_7 and R_1 is $-NHNH_2$ then R_7 is not alkyl; and

(iv) when R_3 is OR_7 , R_1 is $N(R_7)N(R_7)R_9$ and R_9 is $C(O)R_{10}$ where R_{10} is alkyl, then R_7 is not hydrogen; and

(v) at least one heteroaryl group is present.

84. (amended) The method as claimed in claim 83, wherein the said compound is selected from the group consisting of:

(a) N,N'-bis[3-carbonyl-1-(2-thien-2'-yl-2-oxoethyl)-3-pyridinium] hydrazine dibromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(b) 1-(2-ethoxy-2-oxoethyl)-3-(2-(2-pyridyl)hydrazinocarbonyl) pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

~~(c) 1-(2-ethoxy-2-oxoethyl)-3-(2-(benzoyloxy)ethylamino-carbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof,~~

(d) N,N'-bis[3-carbonyl-1-(2-phenyl-2-oxoethyl)pyridinium]hydrazine dibromide or other pharmaceutially acceptable salts thereof,

~~(e) 1-(2-phenyl-2-oxoethyl)-3-(hydrazinocarbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~

(f) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(g) N,N'-bis[3-carbonyl-1-(2-(2',4'-dichlorophenyl)-2-oxoethyl) pyridinium] hydrazine dibromide or other pharmaceutially acceptable salts thereof,

~~(h) 1-(2-phenyl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof,~~

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

- ~~(i) 1-(2-ethoxy-2-oxoethyl)-3-(methanesulfonylhydrazinocarbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- ~~(j) 1-(2-phenyl-2-oxoethyl)-3-(phenylsulfonylhydrazino-carbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- ~~(k) 1-(2-phenyl-2-oxoethyl)-2-chloro-3-(phenylsulfonylhydrazino-carbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- ~~(l) 1-(2-thien-2'-yl-2-oxoethyl)-4-(2-(benzoyloxy)ethylaminocarbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- ~~(m) 1-(2-(2,4'-dichlorophenyl)-2-oxoethyl)-3-(2-(benzoyloxy)ethylaminocarbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- ~~(n) 1-(2-phenyl-2-oxoethyl)-3-(2-(acetoxy)ethyloxy-carbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- ~~(o) 1-(2-ethoxy-2-oxoethyl)-3-(2-(benzoyloxy)ethyloxy-carbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- ~~(p) 1-(2-phenylamino-2-oxoethyl)-4-(phenylsulfonylhydrazino-carbonyl)pyridinium chloride or other pharmaceutially acceptable salts thereof,~~
- ~~(q) 1-(2-(2,4'-dichlorophenyl)-2-oxoethyl)-3-(2(methoxy)ethyloxycarbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- ~~(r) 1-(2-phenylamino-2-oxoethyl)-3-((benzoyloxy)ethylaminocarbonyl)pyridinium chloride or other pharmaceutially acceptable salts thereof,~~
- (s) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylaminocarbonylhydrazinocarbonyl)pyridinium

bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

~~(t) 1-(2-phenyl-2-oxoethyl)-3-(2-(acetoxy)-ethylaminocarbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~

~~(u) 1-(2-phenylamino-2-oxoethyl)-3-(phenylsulfonylhydrazinocarbonyl)pyridinium chloride or other pharmaceutially acceptable salts thereof,~~

~~(v) 1-(2-phenylamino-2-oxoethyl)-3-((4-methylphenyl)sulfonylhydrazinocarbonyl)pyridinium chloride or other pharmaceutially acceptable salts thereof,~~

~~(w) 1-(2-phenyl-2-oxoethyl)-3-(2-(benzoyloxy)ethyloxy-carbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~

(x) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylcarbonylhydrazinocarbonyl)pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

~~(y) 1-(2-ethoxy-2-oxoethyl)-3-((phenylmethyl)sulfonylhydrazinocarbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~

~~(z) 1-(2-phenyl-2-oxoethyl)-3-((phenylmethyl)sulfonylhydrazinocarbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~

(aa) N, N' - bis [3-carbonyl-1-(2-furan-2'-yl-2-oxoethyl)pyridinium] hydrazine dibromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(ab) N,N'-bis [3-carbonyl-1-(2-thien-2'-yl-2-oxoethyl)pyridinium] hydrazine dichloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(ac) N,N'-bis-[3-carbonyl-1-(2-cyclopropylamino-2-oxoethyl)pyridinium] hydrazine dichloride or other pharmaceutially acceptable salts thereof,

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

~~(ad) 1-(2',4'-dichlorophenyl-2-oxoethyl)-3-(2-methoxyethyl-aminocarbonyl)-pyridinium bromide or other pharmaceutially acceptable salts thereof;~~

~~(ae) 1-(2-thien-2'-yl-2-oxoethyl)-3-((2-methoxy-ethyl)-amino-carbonyl)-5-bromo-pyridinium chloride or other pharmaceutially acceptable salts thereof;~~

(af) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(ag) 1-(2-thien-2'-yl-2-oxoethyl)-3-(2-(2-chloro-3-pyridoylhydrazinocarbonyl) – pyridinium chloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

~~(ah) 1-(2-cyclopropylamino-2-oxoethyl)-3-(2-methoxyethylaminocarbonyl) – pyridinium chloride or other pharmaceutially acceptable salts thereof;~~

~~(ai) 1-(2-isopropylamino-2-oxoethyl)-3-(2-methylsulfonylhydrazinocarbonyl)-pyridinium chloride or other pharmaceutially acceptable salts thereof;~~

~~(aj) 1-(2-phenylamino-2-oxo-ethyl)-3-({2-(1-oxo-3-cyclohexyl)-ethyl}-hydrazinocarbonyl)-pyridinium bromide or other pharmaceutially acceptable salts thereof;~~

~~(ak) 1-(2-thien-2'-yl-2-oxoethyl)-3-[2-(benzoyleoxy)ethylamino-carbonyl]-pyridinium bromide or other pharmaceutially acceptable salts thereof;~~

~~(al) 1-(4-ethoxy-2,4-dioxobutyl)-3-(2-(benzoxyloxy)ethylamino-carbonyl)-pyridinium chloride or other pharmaceutially acceptable salts thereof;~~

(am) 1-(2-thien-2'-yl-2-oxoethyl)-3-[1-oxo-1-(2-methoxy carbonyl) pyridyl] hydrazino pyridinium chloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(an) 1-[1-(2-thien-2'-yl-2-oxoethyl)-5-aminocarbonyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-

yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other ~~pharmaceutially~~
pharmaceutically acceptable salts thereof,

(ao) 1-(2-thien-2'-yl-2-oxoethyl)-3-(trifluoromethanesulfonyl hydrazino carbonyl) - pyridinium
bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(ap) 1-[1-(2-thien-2'-yl-2-oxoethyl)-6-methyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-
oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other ~~pharmaceutially~~
pharmaceutically acceptable salts thereof,

(aq) N,N'-bis[3-carbonyl-1-(2-(5-methyl-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine
dichloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(ar) N,N'-bis[3-carbonyl-1-(2-(5-chloro-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine
dichloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(as) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-6-methyl pyridinium
bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(at) N,N'-bis[3-carbonyl-1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)pyridinium] hydrazine dichloride
or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

~~(au) 1-(2-phenylamino-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium chloride or other
pharmaceutially acceptable salts thereof,~~

(av) 1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium
bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(aw) 1-(2-(5-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium
chloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

(ax) 1-(2-(5-chloro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(ay) 1-(2-thien-2'-yl-2-oxoethyl)-3-(ethoxycarbonyl hydrazino carbonyl) pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(az) 1-(2-thien-2'-yl-2-oxoethyl)-3-(isopropylsulfonyl hydrazino carbonyl) pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(ba) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-5-bromo pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

~~(bb) 1-(2-(2-ethoxy carbonyl pyrrolidin-1-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutially acceptable salts thereof,~~

(bc) 1-(2-(5-methyl-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

~~(bd) 1-(2-(4-carboethoxy-thiazolidin-3-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutially acceptable salts thereof,~~

~~(be) 1-(2-(4-benzyl piperidin-1-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,~~

(bf) N,N'-(bis[3-carbonyl-1-(2-(2-ethoxycarbonyl pyrrolidin-1-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

~~(bg) 1-(2-phenylamino-2-oxoethyl)-4-[2-(benzoyloxy)-ethylamino-carbonyl] pyridinium chloride or other pharmaceutically acceptable salts thereof,~~

(bh) 1-(2-thien-2(-yl)-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appln. No. 09/995,731

pharmaceutically acceptable salts thereof, and

(bi) 1-(2-thien-2(-yl-2-oxoethyl)-3-(p-methoxy phenyl sulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof;

~~(bj) 1-(2-ethoxy 2-oxoethyl)-3-(phenyl aminocarbonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(bk) 1-(2-ethoxy 2-oxoethyl)-3-(p-toluene sulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(bl) 1-(2-phenyl 2-oxoethyl)-3-(phenylamino carbonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(bm) 1-(2-phenylamino 2-oxoethyl)-3-(benzyl sulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof;~~

~~(bn) 1-(2-phenyl 2-oxoethyl)-4-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(bo) 1-(2-phenyl 2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(bp) 1-(2-ethoxy 2-oxoethyl)-4-[2-(benzoyloxy) ethyl amino carbonyl] pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(bq) 1-(2-ethoxy 2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(br) 1-(2-phenyl 2-oxoethyl)-3-(p-methoxyphenyl sulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

~~(bs) 1 (2-phenyl-2-oxoethyl)-4-[2-(benzoyloxy)ethylamino-carbonyl]pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(bt) 1 (2-ethoxy-2-oxoethyl)-4-(p-methanesulfonylhydrazino-carbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(bu) 3-carboxylamino-1-(2-(2,4-dichlorophenyl)-2-oxoethyl)pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(bv) 3-(tetrahydrobenzothiazol-2-yl)aminocarbonyl-1-(2-(2,4-dichlorophenyl)-2-oxoethyl)pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(bw) 1 (2-phenyl-2-oxoethyl)-3-((2-hydroxyethyl)aminocarbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(bx) 3-carboxylamino-1-(2-thien-2'-yl-2-oxoethyl)pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(by) 1 (2-phenyl-2-oxoethyl)-3-((p-sulfonamidophenylene)aminocarbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(bz) 1 (2-ethoxy-2-oxoethyl)-3-((acceptable salts thereof,~~

~~(ch) 1 (2-(2,4-dichlorophenyl)-2-oxoethyl)-3-(n-butoxycarbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(ci) 1 (2-(2,4-dichlorophenyl)-2-oxoethyl)-3-(n-butylamino-carbonyl)pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(ej) 1 (2-phenyl-2-oxoethyl)-3-(1-phenyl-1-oxomethyl)pyridinium bromide or other~~

~~pharmaceutically 2-hydroxyethyl)-aminocarbonyl)-pyridinium bromide or other
pharmaceutically acceptable salts thereof;~~

~~(ea) 1-(2-phenyl-2-oxoethyl)-3-(isopropylloxycarbonyl)-pyridinium bromide or other
pharmaceutically acceptable salts thereof;~~

~~(eb) 1-(2-oxopropyl)-3-((2-hydroxyethyl)-aminocarbonyl)-pyridinium chloride or other
pharmaceutically acceptable salts thereof;~~

~~(ec) 1-(2-thien-2'-yl-2-oxoethyl)-3-((2-hydroxyethyl)-aminocarbonyl)-pyridinium bromide or
other pharmaceutically acceptable salts thereof;~~

~~(ed) 1-(2-(2,4-dichlorophenyl)-2-oxoethyl)-3-(isopropylloxycarbonyl)-pyridinium bromide or
other pharmaceutically acceptable salts thereof;~~

~~(ee) 1-(2-phenyl-2-oxoethyl)-3-((4-methylthiazol-2-yl)-aminocarbonyl)-pyridinium
bromide or other pharmaceutically acceptable salts thereof;~~

~~(ef) 1-(2-phenylamino-2-oxoethyl)-3-(n-butylloxycarbonyl)-pyridinium chloride or other
pharmaceutically acceptable salts thereof;~~

~~(eg) 1-(2-phenylamino-2-oxoethyl)-3-((2-hydroxyethyl)-aminocarbonyl)-pyridinium
chloride or other pharmaceutically acceptable salts thereof and~~

~~(ek) 1-(2-phenyl-2-oxoethyl)-3-(methoxycarbonyl)-pyridinium bromide or other
pharmaceutically acceptable salts thereof.~~

85. (amended) A pharmaceutical composition for inhibiting the formation of AGE in a
mammal comprising the compounds as defined in claim 83 in association with pharmaceutically

acceptable carrier, diluent, excipient or solvent.

86. (amended) The composition as claimed in claim 85, wherein the said compound is selected from the group comprising of:

(a) N,N'-bis[3-carbonyl-1-(2-thien-2'-yl-2-oxoethyl)-3-pyridinium] hydrazine dibromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(b) 1-(2-ethoxy-2-oxoethyl)-3-(2-(2-pyridyl)hydrazinocarbonyl) pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

~~(c) 1-(2-ethoxy-2-oxoethyl)-3-(2-(benzoyloxy)ethylamino-carbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof,~~

(d) N,N'-bis[3-carbonyl-1-(2-phenyl-2-oxoethyl)pyridinium]hydrazine dibromide or other pharmaceutially acceptable salts thereof,

~~(e) 1-(2-phenyl-2-oxoethyl)-3-(hydrazinocarbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~

(f) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(g) N,N'-bis[3-carbonyl-1-(2-(2',4'-dichlorophenyl)-2-oxoethyl) pyridinium] hydrazine dibromide or other pharmaceutially acceptable salts thereof,

~~(h) 1-(2-phenyl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof,~~

~~(i) 1-(2-ethoxy-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof,~~

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

- (j) ~~1-(2-phenyl-2-oxoethyl)-3-(phenylsulfonylhydrazino-carbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- (k) ~~1-(2-phenyl-2-oxoethyl)-2-chloro-3-(phenylsulfonylhydrazino-carbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- (l) ~~1-(2-thien-2'-yl-2-oxoethyl)-4-(2-(benzoyloxy)ethylaminocarbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- (m) ~~1-(2-(2,4'-dichlorophenyl)-2-oxoethyl)-3-(2-(benzoyloxy)ethylaminocarbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- (n) ~~1-(2-phenyl-2-oxoethyl)-3-(2-(acetoxo)ethyloxy)carbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- (o) ~~1-(2-ethoxy-2-oxoethyl)-3-(2-(benzoyloxy)ethyloxy carbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- (p) ~~1-(2-phenylamino-2-oxoethyl)-4-(phenylsulfonylhydrazino-carbonyl)pyridinium chloride or other pharmaceutially acceptable salts thereof,~~
- (q) ~~1-(2-(2,4'-dichlorophenyl)-2-oxoethyl)-3-(2(methoxy)ethyloxy carbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- (r) ~~1-(2-phenylamino-2-oxoethyl)-3-((benzoyloxy)ethylaminocarbonyl)pyridinium chloride or other pharmaceutially acceptable salts thereof,~~
- (s) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylaminocarbonyl hydrazinocarbonyl) pyridinium bromide or other pharmaceutially pharmaceutically acceptable salts thereof,
- (t) 1-(2-phenyl-2-oxoethyl)-3-(2-(acetoxo)ethylaminocarbonyl) pyridinium bromide or other

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

~~pharmaceutially acceptable salts thereof,~~

~~(u) 1-(2-phenylamino-2-oxoethyl)-3-(phenylsulfonylhydrazinocarbonyl)pyridinium chloride or other pharmaceutially acceptable salts thereof,~~

~~(v) 1-(2-phenylamino-2-oxoethyl)-3-((4-methylphenyl)sulfonylhydrazinocarbonyl)pyridinium chloride or other pharmaceutially acceptable salts thereof,~~

~~(w) 1-(2-phenyl-2-oxoethyl)-3-(2-(benzyloxy)ethyloxy carbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~

~~(x) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylcarbonylhydrazinocarbonyl)pyridinium bromide or other pharmaceutially pharmaceutically acceptable salts thereof,~~

~~(y) 1-(2-ethoxy-2-oxoethyl)-3-((phenylmethyl)sulfonylhydrazinocarbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~

~~(z) 1-(2-phenyl-2-oxoethyl)-3-((phenylmethyl)sulfonylhydrazinocarbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~

~~(aa) N, N' - bis [3-carbonyl-1-(2-furan-2'-yl-2-oxoethyl)pyridinium]hydrazine dibromide or other pharmaceutially pharmaceutically acceptable salts thereof,~~

~~(ab) N, N' - bis [3-carbonyl-1-(2-thien-2'-yl-2-oxoethyl)pyridinium]hydrazine dichloride or other pharmaceutially pharmaceutically acceptable salts thereof,~~

~~(ac) N, N' - bis [3-carbonyl-1-(2-cyclopropylamino-2-oxoethyl)pyridinium]hydrazine dichloride or other pharmaceutially acceptable salts thereof,~~

~~(ad) 1-(2',4'-dichlorophenyl-2-oxoethyl)-3-(2-methoxyethylaminocarbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

~~(ae) 1-(2-thien-2'-yl-2-oxoethyl)-3-((2-methoxy-ethyl) amino-carbonyl)-5-bromo-pyridinium chloride or other pharmaceutially acceptable salts thereof,~~

(af) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutially pharmaceutically acceptable salts thereof,

(ag) 1-(2-thien-2'-yl-2-oxoethyl)-3-(2-(2-chloro-3-pyridoylhydrazinocarbonyl) -pyridinium chloride or other pharmaceutially pharmaceutically acceptable salts thereof,

~~(ah) 1-(2-cyclopropylamino-2-oxoethyl)-3-(2-methoxyethylaminocarbonyl)-pyridinium chloride or other pharmaceutially acceptable salts thereof,~~

(ai) 1-(2-isopropylamino-2-oxoethyl)-3-(2-methylsulfonylhydrazinocarbonyl)-pyridinium chloride or other pharmaceutially acceptable salts thereof,

~~(aj) 1-(2-phenylamino-2-oxo-ethyl)-3-((2-(1-oxo-3-cyclohexyl)-ethyl)-hydrazinocarbonyl)-pyridinium bromide or other pharmaceutially acceptable salts thereof,~~

~~(ak) 1-(2-thien-2'-yl-2-oxoethyl)-3-[2-(benzoyloxy)ethylamino-carbonyl]-pyridinium bromide or other pharmaceutially acceptable salts thereof,~~

~~(al) 1-(4-ethoxy-2,4-dioxobutyl)-3-(2-(benzoxyleoxy)ethylamino-carbonyl)-pyridinium chloride or other pharmaceutially acceptable salts thereof,~~

(am) 1-(2-thien-2'-yl-2-oxoethyl)-3-[1-oxo-1-(2-methoxy carbonyl) pyridyl] hydrazino pyridinium chloride or other pharmaceutially pharmaceutically acceptable salts thereof,

(an) 1-[1-(2-thien-2'-yl-2-oxoethyl)-5-aminocarbonyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other pharmaceutially pharmaceutically acceptable salts thereof,

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appln. No. 09/995,731

- (ao) 1-(2-thien-2'-yl-2-oxoethyl)-3-(trifluoromethanesulfonyl hydrazino carbonyl) - pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
- (ap) 1-[1-(2-thien-2'-yl-2-oxoethyl)-6-methyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
- (aq) N,N'-bis[3-carbonyl-1-(2-(5-methyl-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
- (ar) N,N'-bis[3-carbonyl-1-(2-(5-chloro-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
- (as) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-6-methyl pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
- (at) N,N'-bis[3-carbonyl-1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)pyridinium] hydrazine dichloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
- (au) 1-(2-phenylamino-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium chloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
- (av) 1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
- (aw) 1-(2-(5-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
- (ax) 1-(2-(5-chloro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

(ay) 1-(2-thien-2'-yl-2-oxoethyl)-3-(ethoxycarbonyl hydrazino carbonyl) pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(az) 1-(2-thien-2'-yl-2-oxoethyl)-3-(isopropylsulfonyl hydrazino carbonyl) pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(ba) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-5-bromo pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

~~(bb) 1-(2-(2-ethoxy carbonyl pyrrolidin-1-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutially acceptable salts thereof,~~

(bc) 1-(2-(5-methyl-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

~~(bd) 1-(2-(4-carboethoxy thiazolidin-3-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutially acceptable salts thereof,~~

~~(be) 1-(2-(4-benzyl piperidin-1-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,~~

(bf) N,N'-(bis[3-carbonyl-1-(2-(2-ethoxycarbonyl pyrrolidin-1-yl)-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutically acceptable salts thereof,

~~(bg) 1-(2-phenylamino-2-oxoethyl)-4-[2-(benzoyloxy) ethylamino carbonyl] pyridinium chloride or other pharmaceutically acceptable salts thereof,~~

(bh) 1-(2-thien-2(-yl)-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof, and

(bi) 1-(2-thien-2(-yl)-2-oxoethyl)-3-(p-methoxy phenyl sulfonyl hydrazino carbonyl) pyridinium

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appln. No. 09/995,731

bromide or other pharmaceutically acceptable salts thereof;

~~(bj) 1 (2-ethoxy-2-oxoethyl)-3-(phenylaminocarbonyl-hydrazino-carbonyl)-pyridinium~~

~~bromide or other pharmaceutically acceptable salts thereof;~~

~~(bk) 1 (2-ethoxy-2-oxoethyl)-3-(p-toluene-sulfonyl-hydrazino-carbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(bl) 1 (2-phenyl-2-oxoethyl)-3-(phenylamino-carbonyl-hydrazino-carbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(bm) 1 (2-phenylamino-2-oxoethyl)-3-(benzyl-sulfonyl-hydrazino-carbonyl)-pyridinium chloride or other pharmaceutically acceptable salts thereof;~~

~~(bn) 1 (2-phenyl-2-oxoethyl)-4-(methanesulfonyl-hydrazino-carbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(bo) 1 (2-phenyl-2-oxoethyl)-3-(phenyl-hydrazino-carbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(bp) 1 (2-ethoxy-2-oxoethyl)-4-[2-(benzoyloxy)-ethyl-amino-carbonyl]-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(bq) 1 (2-ethoxy-2-oxoethyl)-3-(phenyl-hydrazino-carbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(br) 1 (2-phenyl-2-oxoethyl)-3-(p-methoxyphenyl-sulfonyl-hydrazino-carbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(bs) 1 (2-phenyl-2-oxoethyl)-4-[2-(benzoyloxy)-ethyl-amino-carbonyl]-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

~~(bt) 1 (2-ethoxy-2-oxoethyl)-4-(p-methanesulfonyl-hydrazino-carbonyl)-pyridinium-bromide or other pharmaceutically acceptable salts thereof;~~

~~(bu) 3-carboxylamino-1-(2-(2,4-dichlorophenyl)-2-oxoethyl)-pyridinium-bromide or other pharmaceutically acceptable salts thereof;~~

~~(bv) 3-(tetrahydrobenzothiazol-2-yl)-aminocarbonyl-1-(2-(2,4-dichlorophenyl)-2-oxoethyl)-pyridinium-bromide or other pharmaceutically acceptable salts thereof;~~

~~(bw) 1-(2-phenyl-2-oxoethyl)-3-((2-hydroxyethyl)-aminocarbonyl)-pyridinium-bromide or other pharmaceutically acceptable salts thereof;~~

~~(bx) 3-carboxylamino-1-(2-thien-2'-yl-2-oxoethyl)-pyridinium-bromide or other pharmaceutically acceptable salts thereof;~~

~~(by) 1-(2-phenyl-2-oxoethyl)-3-((p-sulfonamidophenylene)-aminocarbonyl)-pyridinium-bromide or other pharmaceutically acceptable salts thereof;~~

~~(bz) 1-(2-ethoxy-2-oxoethyl)-3-((2-hydroxyethyl)-aminocarbonyl)-pyridinium-bromide or other pharmaceutically acceptable salts thereof;~~

~~(ca) 1-(2-phenyl-2-oxoethyl)-3-(isopropoxyloxycarbonyl)-pyridinium-bromide or other pharmaceutically acceptable salts thereof;~~

~~(cb) 1-(2-oxopropyl)-3-((2-hydroxyethyl)-aminocarbonyl)-pyridinium-chloride or other pharmaceutically acceptable salts thereof;~~

~~(cc) 1-(2-thien-2'-yl-2-oxoethyl)-3-((2-hydroxyethyl)-aminocarbonyl)-pyridinium-bromide or other pharmaceutically acceptable salts thereof;~~

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

~~(cd) 1 (2 (2,4-dichlorophenyl) 2-oxoethyl) 3-(isopropoxycarbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(ce) 1 (2-phenyl 2-oxoethyl) 3-((4-methylthiazol-2-yl) aminocarbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(cf) 1 (2-phenylamino 2-oxoethyl) 3-(n-butyloxycarbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,~~

~~(cg) 1 (2-phenylamino 2-oxoethyl) 3-((2-hydroxyethyl) aminocarbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,~~

~~(ch) 1 (2 (2,4-dichlorophenyl) 2-oxoethyl) 3-(n-butoxycarbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

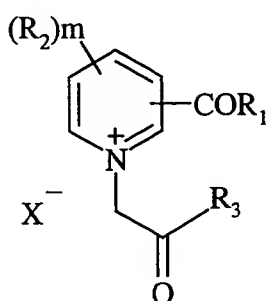
~~(ci) 1 (2 (2,4-dichlorophenyl) 2-oxoethyl) 3-(n-butylamino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(cj) 1 (2-phenyl 2-oxoethyl) 3-(1-phenyl 1-oxomethyl) pyridinium bromide or other pharmaceutically acceptable salts thereof and~~

~~(ek) 1 (2-phenyl 2-oxoethyl) 3-(methoxycarbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof.~~

87. (amended) A method of inhibiting diseases caused by onset of AGE (Advanced Glycation End products) in a mammal which comprises administering an effective amount of a said compound as defined in claim 83 or its pharmaceutically acceptable salts in association with a pharmaceutically acceptable carrier, diluent, excipient or solvent.

89. (amended) A method of treating a mammal for conditions requiring simultaneous action of an AGE-breaker, AGE-formation inhibitor and a free radical scavenger which comprise administering an effective amount of a compound of formula (I) or its pharmaceutically acceptable salts,



(I)

in association with a pharmaceutically acceptable carrier, diluent, excipient or solvent,

wherein

R_1 is ~~R_4 , R_5 or $N(R_7)N(R_7)R_9$ and $Y-R_{11}$;~~

R_4 is selected from the group consisting of $N(R_7)R_6O$,

~~$N(R_7)R_6N(R_7)$,~~

~~OR_6O , and $OR_6N(R_7)$;~~

where R_6 is alkyl;

R_5 is selected from the group consisting of alkyl, aryl including heteroaryl, ~~COR_7 , SO_2R_7 ,~~

~~$C(S)NHR_7$, $C(NH)NHR_7$, COR_{10} ,~~

~~$C(O)NHR_7$ and $N(R_7)N=C$~~

~~_____R₁₀~~

where R₇ is selected from the group consisting of H, alkyl and aryl including heteroaryl,
provided R₇ may be the same or different for R₁ and R₃ in the same compound;

R₂ is selected from the group consisting of F, Cl, Br, I, OR₇, NO₂, alkyl, aryl including
heteroaryl, formyl, acyl, C(O)NR₇R₁₀, C(O)OR₇, NR₇R₁₀, N=C(R₇)(R₁₀), SR₇, SO₂NH₂, SO₂
alkyl and SO₂aryl;

m is 0, 1 or 2;

R₃ is selected from the group consisting of R₇, OR₇, N(R₇)(R₁₀), N=C(R₇)(R₁₀), N(R₇)N(R₇)
(R₁₀), N(R₇)N=C(R₇)(R₁₀) and CH(R₇)C(O)R₈

where R₈ is selected from the group consisting of R₇, OR₇ and NR₇R₁₀;

R₉ is selected from the group consisting of hydrogen, alkyl, aryl including heteroaryl, C(O)R₁₀, -
SO₂R₁₀, C(S)NHR₁₀, C(NH)NH(R₁₀) and C(O)NHR₁₀;

R₁₀ is selected from the group consisting of H, alkyl and aryl, including heteroaryl and in each
case may be the same or different from substituent R₇, provided R₁₀ may be the same or different
for R₁ and R₃ in the same compound;

~~Y is selected from oxygen, NH, NR₁₂ and null~~

~~R₁₁ and R₁₂ are independently selected from hydrogen, alkyl and aryl~~

X is selected from the group consisting of a halide ion, acetate ion, perchlorate ion, sulfonate ion,
oxalate ion, citrate ion, tosylate ion, maleate ion, mesylate ion, carbonate ion, sulfite ion,
phosphoric hydrogen ion, phosphonate ion, phosphate ion, ~~BF₄~~- BF₄⁻ and ~~PF₆~~- PF₆⁻;

with proviso that,

- (i) when two alkyl groups are present on the same carbon or nitrogen, they may be linked together to form a cyclic structure;
- (ii) the nitrogen of heteroaryl ring of R₁₀, when present, may be quaternized;
- (iii) when R₃ is OR₇ and R₁ is -NHNH₂ then R₇ is not alkyl; ~~and~~
- (iv) when R₃ is OR₇, R₁ is N(R₇)N(R₇)R₉ and R₉ is C(O)R₁₀ where R₁₀ is alkyl, then R₇ is not hydrogen; and
- (v) at least one heteroaryl group is present.

90. (amended) The method as claimed in claim 89, wherein said compound is selected from the group consisting of:

- (a) N,N'-bis[3-carbonyl-1-(2-thien-2'-yl-2-oxoethyl)-3-pyridinium] hydrazine dibromide or other pharmaceutially pharmaceutically acceptable salts thereof,
- (b) 1-(2-ethoxy-2-oxoethyl)-3-(2-(2-pyridyl)hydrazinocarbonyl) pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
- (c) ~~1-(2-ethoxy-2-oxoethyl)-3-(2-(benzoyloxy)ethylamino-carbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- (d) N,N'-bis[3-carbonyl-1-(2-phenyl-2-oxoethyl)pyridinium]hydrazine dibromide or other pharmaceutially acceptable salts thereof,
- (e) ~~1-(2-phenyl-2-oxoethyl)-3-(hydrazinocarbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- (f) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other pharmaceutially pharmaceutically acceptable salts thereof,

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

- (g) N,N'-bis[3-carbonyl-1-(2-(2',4'-dichlorophenyl)-2-oxoethyl) pyridinium] hydrazine dibromide or other pharmaceutially acceptable salts thereof,
- ~~(h) 1-(2-phenyl-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- ~~(i) 1-(2-ethoxy-2-oxoethyl)-3-(methanesulfonyl hydrazinocarbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- ~~(j) 1-(2-phenyl-2-oxoethyl)-3-(phenylsulfonylhydrazino carbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- ~~(k) 1-(2-phenyl-2-oxoethyl)-2-chloro-3-(phenylsulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- ~~(l) 1-(2-thien-2'-yl-2-oxoethyl)-4-(2-(benzoyloxy) ethyl aminocarbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- ~~(m) 1-(2-(2',4'-dichlorophenyl)-2-oxoethyl)-3-(2-(benzoyloxy) ethylaminocarbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- ~~(n) 1-(2-phenyl-2-oxoethyl)-3-(2-(acetoxy) ethyloxy) carbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- ~~(o) 1-(2-ethoxy-2-oxoethyl)-3-(2-(benzoyloxy) ethyloxy carbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- ~~(p) 1-(2-phenylamino-2-oxoethyl)-4-(phenylsulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutially acceptable salts thereof,~~
- ~~(q) 1-(2-(2',4'-dichlorophenyl)-2-oxoethyl)-3-(2(methoxy) ethyloxy carbonyl) pyridinium~~

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

~~bromide or other pharmaceutially acceptable salts thereof;~~

~~(r) 1-(2-phenylamino-2-oxoethyl)-3-((benzoyloxy) ethylaminocarbonyl) pyridinium chloride or other pharmaceutially acceptable salts thereof;~~

(s) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylaminocarbonyl hydrazinocarbonyl) pyridinium bromide or other pharmaceutially pharmaceutically acceptable salts thereof,

~~(t) 1-(2-phenyl-2-oxoethyl)-3-(2-(acetoxy) ethylaminocarbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof;~~

~~(u) 1-(2-phenylamino-2-oxoethyl)-3-(phenyl sulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutially acceptable salts thereof;~~

~~(v) 1-(2-phenylamino-2-oxoethyl)-3-((4-methylphenyl)sulfonyl hydrazinocarbonyl) pyridinium chloride or other pharmaceutially acceptable salts thereof;~~

~~(w) 1-(2-phenyl-2-oxoethyl)-3-(2-(benzoyloxy)ethyloxy carbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof;~~

(x) 1-(2-thien-2'-yl-2-oxoethyl)-3-(phenylcarbonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutially pharmaceutically acceptable salts thereof,

~~(y) 1-(2-ethoxy-2-oxoethyl)-3-((phenylmethyl)sulfonyl hydrazino carbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof;~~

~~(z) 1-(2-phenyl-2-oxoethyl)-3-((phenylmethyl)sulfonyl hydrazino carbonyl)pyridinium bromide or other pharmaceutially acceptable salts thereof;~~

(aa) N, N' - bis [3-carbonyl-1-(2-furan-2'-yl-2-oxoethyl) pyridinium] hydrazine dibromide or other pharmaceutially pharmaceutically acceptable salts thereof,

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

- (ab) N,N'-bis [3-carbonyl -1- (2-thien-2'-yl-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutially pharmaceutically acceptable salts thereof,
- (ac) N,N'-bis-[3-carbonyl-1-(2-cyclopropylamino-2-oxoethyl) pyridinium] hydrazine dichloride or other pharmaceutially acceptable salts thereof,
- ~~(ad) 1 (2',4' dichlorophenyl 2-oxoethyl) 3 (2-methoxyethyl aminocarbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- ~~(ae) 1 (2-thien-2'-yl-2-oxoethyl) 3 ((2-methoxyethyl) amino carbonyl) 5-bromo pyridinium chloride or other pharmaceutially acceptable salts thereof,~~
- (af) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutially pharmaceutically acceptable salts thereof,
- (ag) 1-(2-thien-2'-yl-2-oxoethyl)-3-(2-(2-chloro-3-pyridoylhydrazinocarbonyl) -pyridinium chloride or other pharmaceutially pharmaceutically acceptable salts thereof,
- ~~(ah) 1 (2-cyclopropylamino 2-oxoethyl) 3 (2-methoxyethylaminocarbonyl) pyridinium chloride or other pharmaceutially acceptable salts thereof,~~
- ~~(ai) 1 (2-isopropylamino 2-oxoethyl) 3 (2-methylsulfonylhydrazinocarbonyl) pyridinium chloride or other pharmaceutially acceptable salts thereof,~~
- ~~(aj) 1 (2-phenylamino 2-oxo-ethyl) 3 ({2 (1-oxo-3-cyclohexyl) ethyl} hydrazinocarbonyl)-pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- ~~(ak) 1 (2-thien-2'-yl-2-oxoethyl) 3 [2-(benzoyloxy)ethylamino carbonyl] pyridinium bromide or other pharmaceutially acceptable salts thereof,~~
- ~~(al) 1 (4-ethoxy 2,4-dioxobutyl) 3 (2-(benzoyloxy)ethylamino carbonyl) pyridinium chloride~~

~~or other pharmaceutially acceptable salts thereof,~~

(am) 1-(2-thien-2'-yl-2-oxoethyl)-3-[1-oxo-1-(2-methoxy carbonyl) pyridyl] hydrazino
pyridinium chloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(an) 1-[1-(2-thien-2'-yl-2-oxoethyl)-5-aminocarbonyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-
yl-2-oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other ~~pharmaceutially~~
pharmaceutically acceptable salts thereof,

(ao) 1-(2-thien-2'-yl-2-oxoethyl)-3-(trifluoromethanesulfonyl hydrazino carbonyl) - pyridinium
bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(ap) 1-[1-(2-thien-2'-yl-2-oxoethyl)-6-methyl-3-carbonyl pyridinium]-2-[1-(2-thien-2'-yl-2-
oxoethyl)-3-carbonyl pyridinium] hydrazine dichloride or other ~~pharmaceutially~~
pharmaceutically acceptable salts thereof,

(aq) N,N'-bis[3-carbonyl-1-(2-(5-methyl-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine
dichloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(ar) N,N'-bis[3-carbonyl-1-(2-(5-chloro-thien-2-yl)-2-oxoethyl) pyridinium] hydrazine
dichloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(as) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-6-methyl pyridinium
bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

(at) N,N'-bis[3-carbonyl-1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)pyridinium] hydrazine dichloride
or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,

~~(au) 1-(2-phenylamino-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium chloride or other
pharmaceutially acceptable salts thereof,~~

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

- (av) 1-(2-(4-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
- (aw) 1-(2-(5-nitro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
- (ax) 1-(2-(5-chloro-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
- (ay) 1-(2-thien-2'-yl-2-oxoethyl)-3-(ethoxycarbonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutially acceptable salts thereof,
- (az) 1-(2-thien-2'-yl-2-oxoethyl)-3-(isopropylsulfonyl hydrazino carbonyl) pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
- (ba) 1-(2-thien-2'-yl-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl)-5-bromo pyridinium bromide or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
- ~~(bb) 1-(2-(2-ethoxy carbonyl pyrrolidin-1-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutially acceptable salts thereof,~~
- (bc) 1-(2-(5-methyl-thien-2-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other ~~pharmaceutially~~ pharmaceutically acceptable salts thereof,
- ~~(bd) 1-(2-(4-carboethoxy thiazolidin-3-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutially acceptable salts thereof,~~
- ~~(be) 1-(2-(4-benzyl piperidin-1-yl)-2-oxoethyl)-3-(methanesulfonyl hydrazino carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,~~
- (bf) N,N' (-bis[3-carbonyl-1-(2-(2-ethoxycarbonyl pyrrolidin-1-yl)-2-oxoethyl) pyridinium]

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

hydrazine dichloride or other pharmaceutically acceptable salts thereof,

~~(bg) 1-(2-phenylamino-2-oxoethyl)-4-[2-(benzoyloxy)ethylamino-carbonyl]~~

~~pyridinium chloride or other pharmaceutically acceptable salts thereof,~~

(bh) 1-(2-thien-2(-yl-2-oxoethyl)-3-(phenyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof, and

(bi) 1-(2-thien-2(-yl-2-oxoethyl)-3-(p-methoxy phenyl sulfonyl hydrazino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof;

~~(bj) 1-(2-ethoxy-2-oxoethyl)-3-(phenyl aminocarbonyl-hydrazino-carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(bk) 1-(2-ethoxy-2-oxoethyl)-3-(p-toluene-sulfonyl hydrazino-carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(bl) 1-(2-phenyl-2-oxoethyl)-3-(phenylamino-carbonyl hydrazino-carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(bm) 1-(2-phenylamino-2-oxoethyl)-3-(benzyl-sulfonyl hydrazino-carbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof,~~

~~(bn) 1-(2-phenyl-2-oxoethyl)-4-(methanesulfonyl hydrazino-carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(bo) 1-(2-phenyl-2-oxoethyl)-3-(phenyl hydrazino-carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

~~(bp) 1-(2-ethoxy-2-oxoethyl)-4-[2-(benzoyloxy)ethyl-amino-carbonyl] pyridinium bromide or other pharmaceutically acceptable salts thereof,~~

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

~~(bq) 1 (2-ethoxy-2-oxoethyl)-3-(phenylhydrazino-carbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(br) 1 (2-phenyl-2-oxoethyl)-3-(p-methoxyphenyl-sulfonyl-hydrazino-carbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(bs) 1 (2-phenyl-2-oxoethyl)-4-[2-(benzoyloxy)-ethyl-amino-carbonyl]-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(bt) 1 (2-ethoxy-2-oxoethyl)-4-(p-methanesulfonyl-hydrazino-carbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(bu) 3-carboxylamino-1-(2-(2,4-dichlorophenyl)-2-oxoethyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(bv) 3-(tetrahydrobenzothiazol-2-yl)-aminocarbonyl-1-(2-(2,4-dichlorophenyl)-2-oxoethyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(bw) 1 (2-phenyl-2-oxoethyl)-3-((2-hydroxyethyl)-aminocarbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(bx) 3-carboxylamino-1-(2-thien-2'-yl-2-oxoethyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(by) 1 (2-phenyl-2-oxoethyl)-3-((p-sulfonamidophenylene)-aminocarbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(bz) 1 (2-ethoxy-2-oxoethyl)-3-((2-hydroxyethyl)-aminocarbonyl)-pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appl. No. 09/995,731

~~(ca) 1 (2-phenyl 2-oxoethyl) 3 (isopropylloxycarbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(cb) 1 (2-oxopropyl) 3 ((2-hydroxyethyl) aminocarbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof;~~

~~(cc) 1 (2-thien-2'-yl 2-oxoethyl) 3 ((2-hydroxyethyl) aminocarbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(cd) 1 (2 (2,4-dichlorophenyl 2-oxoethyl) 3 (isopropylloxycarbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(ce) 1 (2-phenyl 2-oxoethyl) 3 ((4-methylthiazol-2-yl) aminocarbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(cf) 1 (2-phenylamino 2-oxoethyl) 3 (n-butylloxycarbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof;~~

~~(cg) 1 (2-phenylamino 2-oxoethyl) 3 ((2-hydroxyethyl) aminocarbonyl) pyridinium chloride or other pharmaceutically acceptable salts thereof;~~

~~(ch) 1 (2 (2,4-dichlorophenyl) 2-oxoethyl) 3 (n-butoxycarbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(ci) 1 (2 (2,4-dichlorophenyl) 2-oxoethyl) 3 (n-butylamino carbonyl) pyridinium bromide or other pharmaceutically acceptable salts thereof;~~

~~(cj) 1 (2-phenyl 2-oxoethyl) 3 (1-phenyl 1-oxomethyl) pyridinium bromide or other pharmaceutically acceptable salts thereof and~~

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Appln. No. 09/995,731

~~(ek) 1-(2-phenyl-2-oxoethyl)-3-(methoxycarbonyl)pyridinium bromide or other
pharmaceutically acceptable salts thereof.~~